THE IMPACT OF EXERCISE ON HEMATOPOIETIC STEM CELL PATIENTS

by

Randi Hoffmann

A dissertation submitted to the faculty of
The University of Utah
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

College of Nursing

The University of Utah

August 2013

The University of Utah Graduate School

STATEMENT OF DISSERTATION APPROVAL

The dissertation of Randi Jo Hoffmann

has been approved by the following committee members:

Kathi Mooney, Chair — 12-3-12 (Date Approved)

Erin Rothwell, Member — 12-3-12 (Date Approved)

Bob Wong, Member — 12-3-12 (Date Approved)

Paul LaStayo, Member — 12-3-12 (Date Approved)

Debra Barton, Member — 12-17-12 (Date Approved)

and by Maureen Keefe, Dean of

the College of Nursing

and by Donna M. White, Interim Dean of The Graduate School.

ABSTRACT

Exercise studies with patients undergoing hematopoietic stem cell transplantation (HSCT) show promising benefits in physical performance and fatigue. However, small sample sizes, lack of randomization, and heterogeneity of settings limit translation of findings into clinical practice.

The aims of this randomized control trial were to (a) determine the feasibility and rate of adherence to a supervised exercise intervention during the active phase of HSCT, and (b) examine the intervention impact on functional capacity, fatigue, perceived exertion, muscular strength, cardiovascular endurance and pulmonary status. An additional aim examined the contribution of the Theory of Planned Behavior (TPB), which includes attitudes subjective norms and perceived behavioral control, in explaining exercise behavior.

Sixty participants were randomly assigned to either the exercise intervention (resistance and aerobic exercise for 1 hour three times/week) or the attention control group (patient education group for 1 hour three times/week). The average participant was Caucasian, age 55 and a candidate for autologous or allogeneic transplant. Participants were followed from initial stem cell collection through recovery of their white count, typically for 6 weeks.

The adherence rate to attendance at the exercise program was 79.63%. There was no attrition. Compared to the attention control, the exercise intervention showed a significant difference on functional performance (p = .041), fatigue (p = .041), cardiovascular and pulmonary status (p = <.001). The overall model of TPB contributed 20.3% of the variance in exercise behavior. While no individual variable was found to predict exercise on its own, perceived behavioral control (p = .09) and intention (p = .19) trended towards significance.

This study provides support for the benefits of an exercise program during the active treatment phase of HSCT. Nurses, and other health care professionals, should consider implementing exercise programs to maintain and potentially improve functional outcomes for patients during the active phase of HSCT. While adherence to exercise was only partially explained by TPB, the theory offers insight into factors that might be important to exercise adherence and areas to emphasize in coaching patients about exercise during stem cell transplant.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ACKNOWLEDGMENTS

My deepest gratitude goes first to my husband, William Neville, who has supported me throughout my entire doctoral journey. His confidence and understanding has energized me to carry on.

I wish to acknowledge the support and faith of my parents, John and Phyllis Hoffmann. A special thank you goes to Joshua Neville, a key family member and a faithful friend. Anne Leu is also worthy of my gratitude; her eye for detail, patience and dedication is appreciated.

My research and dissertation would not have been possible without the patience and advice of my committee: Kathi Mooney, Deb Barton, Paul Lastayo, Bob Wong and Erin Rothwell.

Finally, I wish to acknowledge the patients who participated in this study. They inspire and amaze me daily.

This research was funded in part by a doctoral scholarship from the American Cancer Society.

CHAPTER 1

INTRODUCTION

Statement of the Problem

Each year over 50,000 hematopoietic stem cell transplants (HSCT) are performed worldwide. Approximately, 25,000 allogeneic transplants are done annually along with over 30,000 autologous and cord blood transplants (Gratwohl et al., 2010). HSCT is considered a curative treatment for some hematological disorders such as Acute Myelogenous Leukemia, as well as some bone marrow failures (Russell et al., 1996; Russell, Brown et al., 1997; Russell, Desai et al., 1997; Russell et al., 1999). In other cases, transplant can impart good outcomes with a longer life expectancy. In many cases, it is the preferred treatment such as for Aplastic Anemia, Chronic Myelogenous Leukemia and some immune and genetic disorders.

Improvements in transplant technology and after care allow for increased survival rates. While there are thousands of survivors of stem cell transplant alive currently, we know that these patients face multiple challenges throughout their treatment and recovery course. Pretransplant status is often compromised in a substantial number of patients prior to transplant secondary to inactivity, side effects from medications, chemo-therapy or the disease itself. Respiratory, skeletal muscle strength and maximal exercise capacity is reduced (White, Miller, & Ryan, 2005), making recovery of physical function even more demanding. Approximately 40-50% of patients continue to experience physical, psychological, and psychosocial stress up to 5 or more years after transplant (Bhatia et al., 2007), mortality rates twice as high as that of the general population (Bhatia et al., 2007). These patients continue to live with many issues that impact their health and quality of life.

The benefits of physical activity on functional performance, diminished symptoms, and improved quality of life in cancer patients are well established (Courneya, Friedenreich, Arthue, & Bobick, 1999; Galvao & Newton, 2005; Knols, Asronson, Uebelhart, Fransen, & Aufdemkampe, 2005; Stevinson, Lawler, & Fox, 2004). The research in exercise with patients undergoing hematopoietic stem cell transplantation shows similar results such as improved physical function, decreased fatigue, and enhanced quality of life (Wiskemann & Huber, 2008). There is consistent evidence that exercise is safe and provides modest benefits with stem cell transplant patients. Yet many studies are limited in sample size, lack randomization, and were undertaken in a variety of medical contexts. There remains no consensus regarding type and dose of activity and no seminal study that dictates the integration of an exercise program into the treatment regimen of these patients. There clearly is a need for additional research to support a large randomized clinical trial to validate the positive results of previous study and pave the way to the establishment of structured exercise therapy into the medical management of stem cell transplant patients.

While many of the studies document improvements to physical endurance, strength, and quality of life, few have provided interventions during actual treatment and the immediate post transplant recovery period (Cunningham et al., 1986; Dimeo et al., 1996; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; Dimeo et al., 2003; Kim &

Kim, 2006). These studies included either autologous transplant patients or allogeneic. Only one study to date has utilized an intervention during the treatment phase (Baumann, Kraut, Schule, Bloch, & Fauser, 2010) and included both allogeneic and autologous patients. Physical activity during this period of time is key to counteracting the effects of prolonged bed rest, such as muscle atrophy, cachexia, pneumonia, and loss of physical function.

Since we know that these patients continue to struggle over the long term with recovery of physical function, it is essential (Knols et al., 2005; Stevinson et al., 2004) to develop interventions that increase adherence to an exercise regimen beyond the initial recovery period. This is the reason we chose to examine the utility of the Theory of Planned Behavior (TPB). No study to date has utilized a theoretical model to guide their research. The Theory of Planned Behavior suggests that an individual's intention is an immediate predictor of physical activity. TPB has performed well in explaining physical activity intentions in numerous populations (Blanchard et al., 2003; Blanchard, Courneya, Rodgers, & Murnaghan, 2002) and may provide some insights into the development of interventions suited to support patients with exercise adherence.

This feasibility study was undertaken to validate previous research as a step to support the development of a larger randomized clinical trial. It evaluated the impact of a supervised exercise intervention versus an attention control group (both autologous and allogeneic transplant patient) during their treatment and immediate post recovery period. Primary outcomes are fatigue, function, muscular strength, and cardio-pulmonary endurance. Tenets of the Theory of Planned Behavior have been included to guide in the understanding of exercise behavior with this population.

Purpose and Specific Aims

The purpose of this study was to examine the relationship between an exercise intervention versus attention control on functional capacity, fatigue, perceived exertion, muscular strength, cardiovascular endurance, and pulmonary status. The study was guided by three aims and a series of research questions.

Aim #1

To test the feasibility (recruitment, adherence, and attrition) of introducing an exercise intervention vs. attention control with patients undergoing hematopoietic stem cell transplantation in a pilot study.

RQ1A: What is the number and percent of eligible patients that will consent, initiate and complete this study?

RQ1B: What is the degree of adherence to the exercise intervention vs. the attention control group?

RQ1C: What are the reasons for nonadherence?

Aim #2

To examine the relationship between the exercise intervention vs. attention control on functional capacity, fatigue, perceived exertion, muscular strength, cardiovascular endurance, and pulmonary status.

RQ2A: To what extent does the exercise intervention vs. attention control improve functional capacity as measured by the Functional Performance Inventory?

RQ2B: To what extent does the exercise intervention vs. attention control decrease fatigue as measured by the Schwartz Cancer Fatigue Scale?

RQ2C: To what extent does the exercise intervention vs. attention control decrease perceived exertion as measured by the Borg Scale of Perceived Exertion?

RQ2D: To what extent does the exercise intervention vs. the attention control group improve muscular strength as measured by the hand-held grip dynamometer and the step ascent test?

RQ2E: To what extent does the exercise intervention vs. the attention control group improve cardiovascular endurance and pulmonary status as measured by the 6-minute walk test?

Aim #3

To examine how attitudes, intention to exercise, subjective norms, and perceived behavioral control (based on the Theory of Planned Behavior) influence exercise behavior.

RQ3A: Does intention influence exercise behavior?

RQ3B: Does perceived behavioral control influence exercise behavior?

RQ3C: Does attitude influence exercise behavior?

RQ3D: Do subjective norms influence exercise behavior?

Summary of Literature Review

All transplant patients, both autologous (from the patient) and allogeneic (donated by another individual) are at risk for complications during and after treatment. In general, autologous transplantations are thought to be less complicated and are the most common type of transplant. Both groups of patients typically have had previous treatments which can predispose them to having diminished physical status prior to transplant. Physical inactivity and prolonged bed rest can have serious consequences such as reduced bone density and increased risk of thromboembolism (Dimeo, 2001). Potential cardiopulmonary effects include orthostasis and postural hypotension (Illman, Stiller, & Williams, 2000). Respiratory skeletal muscle strength and maximal exercise capacity is reduced in a substantial percentage of patients prior to allogeneic transplant (Morishita et al., 2011; White et al., 2005). Return to work, fatigue, depression, and distress related to treatment or disease can continue for up to 5 years or more after treatment (Syrjala, Chapko, Vitaliano, Cummings, & Sullivan, 1993; Syrjala et al., 2004). These limitations are often present prior to transplant making recovery even more challenging.

Fatigue, a symptom which has been described as prolonged and intense by many survivors (Gruber, Fegg, Buchman, Kolb, & Hiddemann, 2003; Knobel et al., 2000; Oldervoll, Kaasa, Knobel, & Loge, 2003), is seen in both types of transplant patients both prior to transplant and after (Dimeo, 2001; Hacker et al., 2006). While this is a symptom that is seen before transplant, it can continue for up to a year or more (Syrjala et al., 1993; Syrjala et al., 2004). There is a sufficient body of evidence that supports the use of exercise to manage fatigue in cancer patients, as well as stem cell transplant patients. Additional research has been recommended to determine the dose, intensity, and frequency of such interventions (Mitchell, Beck, Hood, Moore, & Tanner, 2007). Of the nonpharmacologic interventions recommended by the National Comprehensive Cancer Network (NCCN) practice guidelines for cancer-related fatigue, exercise has the strongest evidence base for treatment of fatigue (Mock et al., 2000).

It is well established that stem cell transplantation has numerous side effects. When fatigue and physical function are impacted, quality of life is obviously affected. Cytopenias, asthenia, reduced functional capacity, including decreased muscular strength, fatigue, insomnia, and psychological distress are a few of the symptoms that impact quality of life in stem cell transplant patients. Exercise has also shown to improve these symptoms along with physical and emotional well being (Courneya, Keats, & Turner, 2000; Defor, Burns, Gold, & Weisdorf, 2007; Dimeo et al., 2003; Hayes, Davies, Parker, Bashford, & Green, 2004; Wilson, Jacobsen, & Fields, 2005) including the number of days hospitalized (Ono et al., 2010).

In summary, hematopoietic stem cell transplantation (HSCT) can cure some hematologic cancers and impart additional years of life for other patients. Despite cumulative effects of improvements in supportive care, survivors of HSCT will continue to experience side effects of fatigue, limited physical function, and overall diminished quality of life. The continued research with exercise demonstrates that exercise is safe in this population and may reduce these consequences of stem cell transplantation.

Theoretical Framework

This study was guided by the Theory of Planned Behavior (Ajzen & Driver, 1992). This theory suggests that an immediate predictor of physical activity is a person's intention which has three components. Attitude is a positive or negative interpretation of the performance or negative interpretation of the performance of that behavior. Subjective norms are the perceived social pressure one might experience to either perform or not perform the behavior. Perceived behavioral control is the perceived ease or difficulty of engaging in the behavior. Courneya and his colleagues (Courneya, Blanchard, & Laing, 2001; Courneya et al., 1999; Courneya et al., 2000) have conducted five studies using this theory with breast, colorectal, prostate, and one retrospective survey with HSCT patients. Several other studies examined the unique contribution of both instrumental and affective attitude to the prediction of intention in cancer survivors (Rhodes & Courneya, 2003). The tenets of this theory were included in this study to provide insights into exercise behavior in the HSCT population with an eye towards the future development of interventions to assist with exercise adherence.

Research Design

This pilot study utilized an experimental, repeated measures design. Participants were randomly assigned to the intervention or attention control group. A randomization schema was computer generated from the Center of Translational Science at the Mayo Clinic, Rochester, Minnesota.

Setting and Sample

Sixty participants were drawn from a convenience sample of 340 patients at a major cancer center in the upper Midwest. There was no attrition. Inclusion criteria included: age 18 or older; able to speak, read, and write English; and medically cleared by their hematologist. This includes acceptable pulmonary function test (DLCO < 50 %), performance status (0-1 World Health Organization criteria); acceptable bone survey (no acute lesions); echocardiogram (ejection fraction, >45%); infectious disease marker work-up and acceptable renal function. A typical study participant was a Caucasian, married male approximately 54 years old. He is college educated, employed full time, Protestant, and has an approximate income of more than $70,000 annually.

Measures

Variable—Functional Capacity: The Functional Performance Inventory

Functional performance was measured using the Functional Performance Inventory (FPI; Appendix A). This is a self-report measure in which performance is defined as day to day activities that people do to meet basic needs, fulfill usual roles, and maintain health and well-being. While there are many assessment tools to measure function the FPI is chosen because of its unique multidimensional conceptualization of function. Reliability and validity have been demonstrated (Cronbach alpha 0.93). This inventory was administered pre and post as well as weekly. The subscales include: body care, maintaining the household, physical exercise, recreation, spiritual activities, and social interaction. Participants rated various activities under those subscales as do with 1, no difficulty; 2, with some difficulty; 3, with much difficulty; 4, don't due secondary to health reasons.

Variable—Fatigue: The Schwartz Cancer Fatigue Scale

Fatigue was measured using the Schwartz Cancer Fatigue Scale (Appendix B). This is a six-item checklist of adjectives with two components: physical fatigue and mental fatigue. This was chosen over other fatigue scales because it is targeted cancer fatigue. Reliabilities for the total score and the subscales are reported to be greater than 0.80 (Schwartz, 1998). This measure has been well validated in the cancer population. This scale was administered pre and post and weekly. Participants rated various feelings associated with fatigue such as overcome or tired. Ratings were: 1, not at all; 2, a little; 3, moderately; 4, quite a bit; and 5, extremely.

Variable—Perceived Exertion: The Borg Scale of

Perceived Exertion

The Borg Scale of Perceived Exertion (Appendix C) was used to measure perceived exertion and aid with guiding participants in their exercise activity. It is based on the physical sensation a person experiences during physical activity, including increased heart rate, increased respiration, increased perspiration, and muscle fatigue. Although this is a subjective measure, a person's exertion rating may provide a fairly good estimate of the actual heart rate during physical activity (Borg, 1998; Jones et al., 2006, Schneider, Dennehy, & Carter, 2003). A high correlation exists between a person's perceived exertion and the actual heart rate during activity. The Borg Scale of Perceived Exertion is the preferred method to assess intensity among those individuals who take medications such as beta-blockers (Borg, 1998). For this reason, as well as its ease of administration and versatility, the Borg is often used with exercise interventions.

Practitioners generally agree that perceived exertion ratings between 4 and 5 on the Borg Scale suggest that physical activity is being performed at a moderate level of intensity. A scale of 1-10 was used. During activity, the Borg Scale will be used to assign numbers as to how the participant is feeling. This self-monitoring can help guide the patient to either increase the intensity or decrease based on his or her needs.

Variable—Cardio-Pulmonary Endurance:

The Six-Minute Walk

Walk distance tests (12-minute walk test, 6-minute walk test, 2-minute walk test) are measures that can be administered as part of an assessment to determine functional capacity. In a walk distance test, the participant walks back and forth between two markers on a measured course, covering as much ground as possible, and then the distance covered in the allotted time period is recorded. The 6-minute walk distance has been used extensively in evaluating functional capacity in patients undergoing surgery, and in patients with Chronic Obstructive Pulmonary Disease (COPD; Ngaage, Hasney, & Cowen, 2004), heart failure (Spertus et al., 2005), and peripheral arterial disease (Baumann & Arthur, 1997). The distance walked in 6 minutes has been found to strongly correlate with VO2 max and maximum work capacity measured during exercise ergometry (Solway, Brooks, Lacasse, & Thomas, 2001). Procedures for the administration of the 6 minute walk are included in Appendix D.

Variable—Strength: The Step Ascent Test

As an additional measure of physical function used was the test of leg power or the step ascent test. This has demonstrated to strongly relate to functional status in very old and frail men and women (Bean et al., 2002). This intervention includes exercise to stabilize and improve muscle power and may have an impact on functional improvements. Leg power is defined as the weight of an individual times the speed of climbing. This can be estimated from the speed at which an individual can climb a flight of stairs as well as time to perform repeated chair rises (Suzuki, Bean, & Fielding, 2001). In this intervention, participants were timed ascending and descending the same flight of 20 stairs. Both of these measures, while not utilized specifically in the transplant population, have been used with the elderly and frail populations (Henwood & Taaffe, 2006; Working Group on Functional Outcome Measures for Clinical Trials, 2008). This was administered as a pre- and postintervention test.

Variable—Strength: Grip Strength

A hydraulic hand dynamometer (Jamar® hydraulic hand dynamometer; Bissell Healthcare Corporation, Jackson, MI) was used to measure grip strength in participants' dominant hands. Participants held the dynamometer with their elbow flexed and their forearm parallel to the floor and were asked to squeeze as hard as they could. The average of three trials was recorded in kilograms. Procedures used to perform the grip strength evaluation are given in Appendix E.

Variables—Attitude, Perceived Behavioral Control, Subjective Norms and Intention

Aim three variables based on the theory of planned behaviors (Azjen & Driver, 1992) were examined as covariates with a Likert scale previously verified and utilized (Jones et al., 2006). Attitude toward exercise, intention to exercise, perceived behavioral control and subjective norms were assessed at the baseline and after the study.

Procedures

Approval for this study was obtained from the Institutional Review Board at a large midwestern Cancer Center as well as the University of Utah. All participation occurred in the Clinical Research Unit. This is an out-patient unit supported by funding from the Center for Translational Science and was chosen for its research support staff as well as its proximity to the out-patient clinic where patients are seen daily. Advertising for the study was completed with an approved recruitment flyer (Appendix F).

Once participants were found eligible for the study and had consented to be research participants (via general institutional consent) they were contacted by phone by the PI. A previously approved phone script was utilized. If they were interested in participation in this study, a meeting was scheduled for the purpose of providing information on the study and obtaining informed consent if they agreed to participate. The participants would then be randomized to either the intervention group or the control group. The PI and the participants were blinded to this process. This was done via a stratified (to ensure an equal number of autologous vs. allogeneic participants) computer generated program. Data collection was done by the primary investigator. Data were entered and stored in the RedCap data base which is password protected. All data were entered by the PI and double checked prior to entry. All self-report surveys were completed by patients and stored in folders which were coded with no identifying information. These were stored in a locked file cabinet and the PI was the only person with access.

After consenting to the study, both groups were asked to complete both a pre- and postassessment which consisted of demographic information (Appendix G), the Functional Performance Index, the Schwartz Cancer Fatigue Scale, the Godin Leisure Time Questionnaire (Appendix H), and the objective testing of the 6-Minute Walk, the Stair Ascent, and the grip strength test, and a Likert scale assessing attitudes towards exercise, intention to exercise, perceived behavioral control, and subjective norms (Appendix I). This took about 45-60 minutes. Participants were accompanied by the tester for safety reasons. Both groups also completed weekly surveys which included the Godin Leisure Time Questionnaire, the Schwartz Cancer Fatigue Survey, and the Functional Performance Inventory which took approximately 15 minutes. This was done during their scheduled sessions. All questionnaires were administered by the PI. Privacy during questionnaire completion was provided.

Both groups were expected to participate three times per week for approximately 30-60 minutes from the time they collected their stem cells, received their chemotherapy, and through the time of neutrophil engraftment which was defined as an absolute neutrophil count of 0.5 for 3 consecutive days and or 1.0 for 1 day. These sessions were typically scheduled in conjunction with daily out-patient exams for convenience to the participants.

Intervention Group

The intervention group participated three times weekly; they were individually supervised by the PI who is a certified Nurse Practitioner and also completed training at the Rocky Mountain Cancer Rehabilitation Institute. Each session was individualized to meet the needs of the participant’s ability that day. Participants were instructed on the proper use of the equipment including the Thera© Bands. Each session consisted of 20-30 minutes of aerobic exercises (either treadmill or recumbent bicycle) and 20-30 minutes of combined stretching/warm-up/cool down with various levels of resistance exercises with Thera© Bands (biceps/triceps curls, shoulder flexion, abduction, extension) with 10-12 repetitions each. The goal was to exercise at an intensity of 60-75 % of the age-predicted maximum heart rate which was guided by the Borg Scale of Perceived Exertion. Participants were excluded from participation if they were thrombocytopenic (platelet count <20,000), febrile, orthostatic, or did not feel well enough to participate. Weekly questionnaires were administered by the PI. Privacy was provided during completion of the questionnaires. See Table 1, the summary table for the intervention group session.

Control Group

Participants in the attention control group participated in educational sessions that were also individualized and taught and developed by the PI. They will be offered encouragement to follow standard care which is typically to remain as active as possible with no formal exercise program with the usual safety precautions. They had an opportunity to view educational video tapes with a variety of topics such as spirituality, humor, relaxation, nutrition, digestive health, and dealing with side effects. Information on fatigue and exercise will not be included. Topics and examples can be found in Appendix J. Participants were encouraged to engage in physical activity but this was not required. Any physical activity that they engaged in was captured in the weekly Godin Leisure Time Questionnaire. Weekly questionnaires were administered by the PI. Privacy was provided during completion of the questionnaires. See Table 2, the summary table for the control group session.

Data Analysis

Sample size and power analysis was undertaken prior to initiating this study. Using an a priori analysis (Cohen, 1988), the prespecified significance level α, and the population effect size to be detected with the probability 1-B. Utilizing a repeated measures ANOVA, the effect size (F) was set at 0.25, with an alpha error probability of 0.05 and a power alpha/beta ratio of 0.95. The suggested sample size was 44 participants; however, 60 participants were accrued, based on a prediction rate of 30% based on attrition rates of previous study. There was no attrition in this study.

Inferential statistics were used to draw conclusions from the sample tested. The Statistical Package for the Social Sciences (SPSS) version 19 was used to code and tabulate scores and provide summarized values where applicable. Descriptive statistics including frequency counts and percent statistics were computed for the demographic variables. The data were cleaned and screened for missing data and outliers. Frequencies were run for baseline differences; finding none, we proceeded with the analysis. Chi square, Fisher's Exact Test, mixed between-within ANOVA and bivariate correlation were used to test the hypotheses. The assumptions of ANOVA and Pearson bivariate correlation were evaluated prior to the analysis. If the assumptions were not met a nonparametric alternative was used to test the hypotheses.

Significance

Hematopoietic stem cell transplantation has become increasingly successful; however, despite the many advances in supportive care, many survivors remain physically deconditioned and functionally impaired (Hacker et al., 2006). There is increasing evidence that demonstrates that participation in regular physical exercise during and after treatment can improve or at a minimum stabilize those effects. Many transplant programs are now encouraging their patients to engage in physical activity.

This study adds to the body of knowledge in this area in three important ways. One, this study engaged both autologous and allogeneic patients prior to receipt of their chemo-therapy and throughout their immediate recovery. Only one study to date has utilized both autologous and allogeneic patients during this treatment phase and the immediate post transplant recovery phase (Baumann et al., 2010). This is a period when patients are experiencing many significant side effects from chemo-therapy including nausea, diarrhea, diminished nutritional intake, and pancytopenia.

Second, this study showed that participants could exercise at moderate levels of perceived exertion during their transplant and immediate postrecovery (the six time points of this study) based on the Borg Scale. This may give some guidance on dose for future study.

This is important for the development of rehabilitation programs for this population. Multiple efforts now exist to increase the capacity of fitness professionals to serve the unique needs of stem cell transplant patients and cancer patients in general (Schmitz et al., 2011). The knowledge that both endurance and resistance activity can be utilized (albeit at individualized levels) can help professionals make informed choices when working with this population.

Third, this study utilized a theoretical framework. By studying how attitude, intention, perceived behavioral control, and subjective norms influence exercise behavior we gain insights that are useful in the maintenance of physical activity. If included in future research, we can consider the integration of these concepts into the development of an individualized rehabilitation program for stem cell transplant patients.

In summary, this study provides further support for the use of exercise as part of the management of the stem cell transplant patient. It provides evidence that exercise is safe and feasible at a time when many patients are not expected to engage in physical activity. Additional information about the type, timing and dose of exercise will be useful for future research as well the development of rehabilitation programs and fitness professionals. Lastly, gained insights in predictive variables such as intention and perceived behavioral control can be applied to the development of future programming aimed at the maintenance of healthy behaviors and the development of supportive care guidelines for the ongoing recovery of stem cell transplant patients.

Table 1

Session Summary for Intervention Group

Time	Task	Description
5-10 minutes	Warm-up	Gentle stretches Arm raises-head turns-side bends 5 minutes-bike Perceived Exertion (PE) 6-10
10-20 Minutes	Aerobic Work-out	Bike (2 mph) or treadmill (level 1) -monitor HR and PE Adjust accordingly (time and difficulty) (PE 10-12)
15-20 Minutes	Resistance Work-out	Upper body-shoulder flexion-abduction-elbow flexion-extension 10-15 repetitions each Lower Body-min-squats (sit to stand)-heel raises-standing march-hipextension-10-15 repetitions (PE-10-14) Adjust as needed
5-10 Minutes	Cool Down	Treadmill or bike at low PE of 6-10 Gentle stretching (heel cord stretch-hamstring stretch) Encourage fluid intake with complementary beverages

Table 2

Session Summary for Control Group

Time	Task	Description
10-15 Minutes	Introductions	Questions-concerns initiated by patient and or caregiver
15-20 Minutes	Main topic	Can be topic in initiated by patient and or caregiver Or they can choose from a series of topics of prewritten modules and/or videos
5-10 Minutes	Summary	Time for questions and or discussion related to topics
5-10 Minutes	Planning	Time for suggestions for the next session

References

Ajzen, I., & Driver, B. L. (1992). Application of planned behavior to leisure choice. *Journal of Leisure and Rest, 24*(3), 207-224.

Baumann, F. T., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation, 45*, 355-362.

Baumann, H. C., & Arthur, H. M. (1997). Relationship between functional exercise capacity and general quality of life in nonsurgical patients with lower-extremity peripheral arterial disease. *Journal of Vascular Nursing, 15*(1), 21-28.

Bean, J. F., Kiely, D. K., Herman, S., Leveille, S. G., Mizer, K., Frontera, W. R., & Fielding, R. A. (2002). The relationship between leg power and physical performance in mobility-limited older people. *Journal of the American Geriatric Society, 50*, 461-467.

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker, S., Gurney, J. G., . . . Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: Report from the Bone Marrow Transplant Survivor Study. *Blood, 110*(10), 3787-3792.

Blanchard, C., Courneya, K. S., Rodgers, W. M., Fraser, S. N., Murray, T. C., Daub, B., & Black, B. (2003). Is the theory of planned behavior a useful framework for understanding exercise adherence during phase II cardiac rehabilitation? *Journal of Cardiopulmonary Rehabilitation, 23*(1), 29-39.

Blanchard, C., Courneya, K. S., Rodgers, W. M., & Murnaghan, D. M. (2002). Determinants of exercise intention and behavior in survivors of breast and prostate cancer: An application of the Theory of Planned Behavior. *Cancer Nursing, 25*(2), 88-95.

Borg, G. (1998). *Borg's perceived exertion and pain.* Champaign, IL: Human Kinetics.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.

Courneya, K., Blanchard, C. M., & Laing, D. (2001). Exercise adherence in breast cancer survivors training for a dragon boat race competition: A preliminary investigation. *Psycho-oncology, 10*, 444-452.

Courneya, K., Friedenreich, C. M., Arthue, K., & Bobick, T. M. (1999). Understanding exercise motivation in colorectal patients: A prospective study using the theory of planned behavior. *Rehabilitation Psychology, 44*(1), 68-84.

Courneya, K., Keats, M. R., & Turner, A. R. (2000). Social cognitive determinants of hospital-based exercise in cancer patients following high dose chemotherapy and bone marrow transplantation. *International Journal of Behavioral Medicine, 7*(3), 189-203.

Cunningham, B., Morris, G., Cheney, C. L., Buergel, N., Aker, S. N., & Lenssen, P. (1986). Effects of resistive exercise on skeletal muscle in marrow transplant recipients receiving total parental nutrition. *Journal of Parenteral Enteral Nutrition, 10,* 558-563.

Defor, T., Burns, L. J., Gold, E. M., & Weisdorf, D. J. (2007). A randomized trial of the effect of a walking regimen on the functional status of 100 adult allogeneic donor hematopoietic cell transplant patients. *Biology of Blood and Marrow Transplant, 13*(8), 948-955.

Dimeo, F. (2001). Effects of exercise on cancer-related fatigue. *Cancer, 90*(6), 1689-1693.

Dimeo, F., Bertz, H., Finke, J., Fetscher, S., Mertelsmann, R., & Keul, J. (1996). An aerobic exercise program for patients with haematological malignancies after bone marrow transplantation. *Bone Marrow Transplant, 18,* 157-160.

Dimeo, F., Fetscher, S., Lange, W., Mertelsmann, R., & Keul, J. (1997). Efects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood, 90,* 3390-3394.

Dimeo, F., Schwartz, S., Fietz, T., Wanjura, T., Boning, D., & Thiel, E. (2003). Effects of endurance training on the physical performance of patients with hematological malignancies during chemotherapy. *Supportive Care Cancer, 11,* 623-628.

Galvao, D. A., & Newton, R. U. (2005). Review of exercise interventions studies in cancer patients. *Journal of Clinical Oncology, 23*(4), 899-909.

Gratwohl, A., Baldomero, H., Aljurf, M., Pasquini, M. C., Bouzas, L. F., Yoshimi, A., . . . Kodera, Y. (2010). Hematopoietic stem cell transplantation: A global perspective. *Journal of the American Medical Association, 303*(16, 1617-1624.

Gruber, U., Fegg, M., Buchman, M., Kolb, H. F., & Hiddemann, W. (2003). The long-term psychosocial effects of haematopoietic stem cell transplantation. *European Journal of Cancer Care, 12,* 249-256.

Hacker, E., Ferrans, C., Verlen, E., Ravandi, F., Van Besien, K., Gelms, J., & Dieterle, N. (2006). Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncology Nursing Forum, 33*(3), 614-624.

Hayes, S., Davies, P. S., Parker, T., Bashford, J., & Green, A. (2004). Role of a mixed-type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *British Journal of Sports Medicine, 38,* 304-309.

Henwood, T. R., & Taaffe, D. R. (2006). Short-term resistance training and the older adult: The effect of various programmes for the enhancement of muscle strength and functional performance. *Clinical Physiology and Functional Imaging, 26*(5), 305-313.

Illman, A., Stiller, K., & Williams, M. (2000). The prevalence of orthostatic hypotension during physiotherapy treatment with patients with an acute spinal cord injury. *Spinal Cord, 38,* 741-747.

Jones, L., Courneya, K. S., Vallanec, J. K., Ladha, A. B., Mant, M. J., Belch, A. R., & Reiman, T. (2006). Understanding the determinants of exercise intentions in multiple myeloma. *Cancer Nursing, 29*(3), 167-175.

Kim, S., & Kim, H. S. (2006). A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. *European Journal of Cancer Care—English Version, 15,* 453-457.

Knobel, H., Loge, J. H., Nordoy, T., Kolstad, A. L., Especik, T., Kvaloy, S., &. Kaasa, S. (2000). High level of fatigue in lymphoma patients treated with high dose therapy. *Journal of Pain and Symptom Management, 19,* 446-456.

Knols, R., Asronson, N. K., Uebelhart, D., Fransen, J., & Aufdemkampe, G. (2005). Physical exercise in cancer patients during and after medical treatment: A systematic review of randomized and controlled clinical trials. *Journal of Clinical Oncology, 23*(16), 3830-3842.

Mitchell, S., Beck, S. L., Hood, L. E., Moore, K., & Tanner, E. R. (2007). Putting evidence into practice: Evidence-based interventions for fatigue during and following cancer and its treatments. *Clinical Journal of Oncology Nursing, 11*(1), 99-113.

Mock, V., Atkinson, A., Barsevick, A., Cella, D., Cimprich, B., Cleeland, C., . . . Stahl, C. (2000). NCCN practice guidelines for cancer-related fatigue. *Oncology, 14,* 151-161.

Morishita, S., Kaida, K., Ikegame, K., Yoshihara, S., Taniguchi, K., Okada, M., . . . Domen, K. (2011). Impaired physiological function and health-related QOL in patients before hematopoietic stem-cell transplantation. *Supportive Care in Cancer, 20*(4), 821-829.

Ngaage, D. L., Hasney, K., & Cowen, M. E. (2004). The functional impact of an individualized, graded, outpatient pulmonary rehabilitation in end-stage chronic obstructive pulmonary disease. *Heart and Lung, 33*(6), 381-389.

Oldervoll, L., Kaasa, S., Knobel, H., & Loge, J. (2003). Exercise reduces fatigue in chronic fatigued Hodgkins disease survivors—Results from a pilot study. *European Journal of Cancer*, *39,* 57-63.

Ono, I. J., Okamura, A., Matsui, T., Taskekoshi, H., Kurosaka, M., Saura, R., & Shimada, T. (2010). The impact of early rehabilitation on the duration of hospitalization in patients after allogeneic hematopoietic stem cell transplantation. *Transplantation Proceedings, 42*(7), 2740-2744.

Rhodes, R., & Courneya, K. S. (2003). Investigating multiple components of attitude, subjective norm and perceived control: An examination of the theory of planned behavior in the exercise domain. *British Journal of Social Psychology, 42*(pt. 1), 19-36.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1996). Allogeneic blood cell transplants for haematological malignancy: Preliminary comparison of outcomes with bone marrow transplantation. *Bone Marrow Transplant, 17,* 703-708.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1997). Second allogeneic transplants for leukemia using blood instead of bone marrow as a source of hematopoietic cells. *Bone Marrow Transplant, 18,* 501-505.

Russell, J. A., Desai, S., Herbut, B., Brown, C., Luider, J., Ruether, J. D., . . . Klassen, J. (1997). Partially mismatched blood cell transplants for high-risk hematologic malignancy. *Bone Marrow Transplant*, *19*, 861-866.

Russell, J. A., Larratt, L., Brown, C., Turner, A. R., Chaudhry, A., Booth, K., . . . Poon, M. C. (1999). Allogeneic blood stem cell and bone marrow transplantation for acute myelogenous leukemia and myelodysplasia: Influence of stem cell source on outcome. *Bone Marrow Transplant*, *24*, 1177-1183.

Schmitz, K., Courneya, K., Matthews, C., Denmark-Wahnefried, W., Galvao, D., Pinto, B., . . . Schwartz, A. (2011). American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Medicine & Science in Sports and Exercise, 43*(1), 1409-1426.

Schneider, C., Dennehy, C. A., & Carter, S. D. (2003). *Exercise and cancer recovery.* Champaign, IL: Human Kinetics.

Schwartz, A. I. (1998). The Schwartz Cancer Fatigue Scale: Testing, reliability and validity. *Oncology Nursing Forum, 25*(4), 717-722.

Solway, S., Brooks, D., Lacasse, Y., & Thomas, S. (2001). A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest, 119*(1), 256-270.

Spertus, J., Peterson, E., Conard, M. W., Heidenreich, P. A., Krumholz, H. M., Jones, P., . . . Rumsfeld, J. S. (2005). Monitoring clinical changes in patients with heart failure: A comparison of methods. *American Heart Journal, 150*(4), 707-715.

Stevinson, C., Lawlor, D. A., & Fox, K. R. (2004). Exercise interventions for cancer patients: A systematic review of trials. *Cancer Causes Control, 15*(10), 1035-1056.

Suzuki, T., Bean, J. F., & Fielding, R. A. (2001). Muscle power of the ankle flexors predicts functional performance in community-dwelling older women. *Journal of the American Geriatric Society, 49*, 1161-1167.

Syrjala, K. L., Chapko, M. K., Vitaliano, P. P., Cummings, C., & Sullivan, K. M. (1993). Recovery after allogeneic marrow transplantation: Prospective study of predictors of long-term physical and psychosocial functioning. *Bone Marrow Transplantation, 11*(4), 319-327.

Syrjala, K. L., Langer, S. L., Abrams, J. R., Storer, B., Sanders, J. E., Flowers, M. E., & Martin, P. J. (2004). Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. *Journal of the American Medical Association, 291*(19), 2335-2343.

White, A., Miller, K. B., & Ryan, H. F. (2005). Impaired respiratory and skeletal muscle strength in patients prior to hematopoietic stem cell transplantation. *Chest, 128*, 145-152.

Wilson, R., Jacobsen, P. B., & Fields, K. K. (2005). Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. *Bone Marrow Transplant, 35*, 721-727.

Wiskemann, J., & Huber, G. (2008). Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant, 41*, 321-329.

Working Group on Functional Outcome Measures for Clinical Trials. (2008). Functional outcomes for clinical trials in frail older persons: Time to be moving. *Journal of Gerontology, 63A* (2), 160-164.

CHAPTER 2

EXERCISE AND STEM CELL TRANSPLANTATION:

A REVIEW OF THE LITERATURE

Randi Hoffmann, RN, PhD (c)
Mayo Clinic, Rochester, Minnesota

Kathi Mooney, RN, PhD, FAAN
University of Utah—College of Nursing

Debra Barton, RN, PhD, AOCN, FAAN
Mayo Clinic, Rochester, Minnesota

Erin Rothwell, PhD, TRS, CTRS, CRSS
University of Utah—College of Nursing

Paul C. LaStayo, PT, PhD, CHT
University of Utah

Bob Wong, PhD
University of Utah—College of Nursing

Manuscript to be submitted to *Cancer Nursing*

Exercise and Stem Cell Transplantation: A Review

Each year over 50,000 hematopoietic stem cell transplants (HSCT) are performed worldwide. Approximately, 25,000 allogeneic transplants are done annually along with over 30,000 autologous and cord blood transplants (Gratwohl et al., 2010). HSCT is considered a curative treatment for some hematological disorders such as Acute Myelogenous Leukemia, as well as some bone marrow failures (Russell et al., 1996; Russell, Brown, et al., 1997; Russell, Desai, et al., 1997; Russell et al., 1999). In other cases, transplant can impart good outcomes with a longer life expectancy. In many cases, it is the preferred treatment such as for Aplastic Anemia, Chronic Myelogenous Leukemia and some immune and genetic disorders.

The role of exercise in cancer including stem cell transplant patients has demonstrated both physical and psychological benefits (Mock et al., 2000) with recovery. Much of the early work in this area showed a protective and preventative role in terms of the development of cancer. This was particularly true for breast and colon cancer as well as prostate, lung and endometrial cancers. A review done by Courneya, Mackey, and Jones (2000) of 47 published studies suggested that exercise may be an effective intervention for enhancing quality of life in cancer survivors. Multiple other studies have linked increased levels of physical activity with enhanced performance, decreased fatigue and improved quality of life. Many of these studies have utilized cardiovascular training with few using combinations of resistance and aerobic activity (Wilson, Jacobsen, & Fields, 2005; Mello, Tanaka, & Dulley, 2003). Few studies have utilized a theoretical framework in their investigations and most studies included samples that include either exclusively breast cancer patients or samples that were heterogeneous in age, disease and treatment limiting generalizability (Wiskemann & Huber, 2008).

The research in exercise with patients undergoing hematopoietic stem cell transplantation (HSCT) shows similar results to the research in cancer and physical activity. These studies show a benefit in physical performance and decreased fatigue. The majority of the studies show a positive impact of exercise on physiological as well as psychological aspects of recovery.

Exercise intervention programs have been found to be effective in the recovery phase of HSCT patients (Hayes, Davies, Parker, Bashford, & Green, 2004; Hayes, Davies, Parker, Bashford, & Newman, 2004; Kim & Kim, 2006). Some of the outcomes include the effects of exercise interventions on the immune system, changes in body composition, weight, and various psychological traits. Endurance/aerobic exercise programs are the most common form among HSCT patients (Carlson, Smith, Russell, Fibich, & Whittaker, 2006).

In order to understand the trajectory of the impact of exercise on hematopoietic stem cell transplant (HSCT) patients, from pretransplant and beyond recovery, a comprehensive literature review was undertaken. Twenty-five relevant articles were identified and were included in this review, published between 1998 and 2010. The articles included were selected based on the following criteria: (a) the study presented in the English language, and (b) available in online databases including Medline, Cochrane and Cinahl. Key search words included words such as pretransplant status of HSCT patients, HSCT physiological outcomes, HSCT psychological outcomes, exercise recommendations for HSCT patients. The relevant research literature retrieved is reviewed under the following topics: (a) pretransplant status of HSCT patients, (b) quality of life after transplantation, (c) fatigue and exercise, d) physiological/ psychological outcomes of exercise, (e) types of exercises, (f) exercise recommendations, and (g) barriers to exercise.

Pretransplant and Posttransplant Survivorship

Improvements in transplant technology and after care allow for increased survival rates. There are thousands of survivors of stem cell transplant alive today. Throughout recovery from transplant, approximately 40-50% of patients experience physical, psychological and psychosocial stress. Bhatia et al. (2007) reported that while relative mortality decreased with time after HSCT, it remained significantly higher even after 15 years (standardized mortality ratio = 2.2). Relapse of the primary disease (29%) and graft versus host disease (22%) were the leading causes of premature death. At 2 years, post HSCT survivors reported having difficulties holding a job (odds ratio = 13.9). Rovo et al. (2008) looked at 44 survivors of HSCT with a median range of 17.5 years after transplant. In a paired comparison with their donors, survivors showed significantly lower ranks on the norm-based scores for all questions related to physical well-being. These studies support that even when treatments are successful, patients suffer from loss of physical performance, fatigue, distress, emotional problems and immunological and hematological changes (Courneya, Mackey, & McKenzie, 2000). There are additional related toxicities that cause nausea, vomiting, diarrhea, pain, and sepsis which can exacerbate physical and psychological debilitation (Sullivan, 1999; Willenbacker, Mumm, Ruither, Weis, & Bartsch, 1998). Patients report that it can take weeks to months to a year or more to recover from these treatment related morbidities. Many report that they never fully recover. Muscle weakness, diminished cardiac function, fatigue, pain and respiratory complications constitute some of the well documented side effects (Andrykowski et al., 2005; Hayes, Davies, Parker, Bashford, & Newman, 2004).

Studies on HSCT patients are primarily geared after the transplantation and during recovery (Courneya, Mackey, & McKenzie, 2000; DeFor, Burns, Gold, & Weisdorf, 2007; Dimeo, Fetscher, Lnaage, Mertelsmann, & Keul, 1997; Hayes, Davies, Parker, Bashford, & Newman, 2004; Kim & Kim, 2006). Few studies are devoted on the pretransplant status of patients who are going to undergo HSCT; instead, many of the existing studies focus on in-patient, out-patient, or home settings. Few have captured this population prior to chemotherapy and stem cell transplantation.

All four studies reviewed on the pretransplant status of HSCT patients involve both autologous and allogeneic patients. In all studies reviewed, poor pretransplant status was established among HSCT patients prior to transplant (Dimeo, 2001; Illman, Stiller, & Williams, 2000; White, Miller, & Ryan, 2005; Kebriaei et al., 2005). Some of the pretransplant predispositions, diseases, and weaknesses reported included reduced bone density and increased risk of thromboembolism, cardiopulmonary complications, decreased exercise capacity, and co-morbidities.

Allogeneic and autologous patients typically have had previous treatments, which can predispose them to having diminished status prior to transplant. Prolonged immunosuppression and exposure to glucocorticoids are associated with muscle atrophy. Physical inactivity and prolonged bed rest can have serious consequences, such as reduced bone density and increased risk of thromboembolism (Dimeo, 2001). Potential cardiopulmonary effects include orthostatsis and postural hypotension (Illman et al., 2000).

Two studies, White et al. (2005) and Kebriaei et al. (2005), focus on the pretransplant status of HSCT patients. White et al. examined the health condition of pretransplant HSCT patients to understand the trajectory of the health of HSCT patients after the transplantation. Kebriaei et al. focused on the association between pretransplant status and poor outcomes after HSCT.

White et al. (2005) showed that respiratory and skeletal muscle strength and maximal exercise capacity are reduced in a substantial percentage of patients prior to allogeneic transplant. With a prospective observational study of 56 patients, investigators used measures of chemotherapy burden, pulmonary function tests, maximal inspiratory muscle strength, expiratory muscle strength, dominant hand grip, and a 6 minute walk test. They found that all measures were significantly reduced in this population prior to receiving chemotherapy and transplant. Approximately 60% of participants in this study had values less than 80% of predicted scores in all areas. This did not include testing for lower body strength, which can be more severely impacted secondary to immobility. It also did not examine posttransplant respiratory complications and whether or not pretransplant weakness may impact status after transplant. Moreover, it was a single center study. Despite these limitations, this research lays the ground work for further study in this area along with the examination of interventions targeted at the progression of debilitation.

Kebriaei et al. (2005) reviewed the outcomes of 68 adults with Acute Myelogenous Leukemia (AML) and Myelodysplastic Syndrome (MDS) at the time of transplant to confirm recognized risk factors for overall survival and progression-free survival. In addition to the influence of disease status and other co-morbidities, such as graft versus host disease, they found that poor performance status (tested using the Eastern Cooperative Oncology Groups performance scale) were risk factors. A performance status at the time of transplant of two or greater (four is completely disabled) supported an association between pretransplant status and poor outcomes after SCT. Studies have not addressed whether physical activity in the pretreatment phase can prevent further decline in the physical status of stem cell transplant patients.

Quality of Life After Transplantation

It is well documented that stem cell transplantation has numerous side effects that impact the quality of life of patients (Courneya, Mackey, & McKenzie, 2000; Hayes, Davies, Parker, Bashford, & Green, 2004; Morishita et al., 2012). Patients who underwent an allogeneic stem cell transplant were found to have decreased physiological function and health related quality of life after transplantation (Morishita et al., 2012). Cytopenias, asthenia, and reduced functional capacity including decreased muscle strength, fatigue, insomnia, and psychological distress are few of the symptoms that play a role in the diminished quality of life of patients who underwent stem cell transplantation. Exercise has been shown to improve these symptoms along with physical and emotional well-being.

The quality of life of allogeneic HSCT patients is critical 3 years or more after the recovery from transplantation. Physical recovery often occurs before psychological or work recovery (Syrjala et al., 2004). The protracted examination after transplantation is significant because 3 years after a transplant is the start of a critical period wherein HSCT patients are likely to develop diseases and complications (Bhatia et al., 2007). Most studies, however, focused on the immediate recovery period of HSCT patients (Courneya, Mackey, & McKenzie, 2000; DeFor et al., 2007; Hayes, Davies, Parker, Bashford, & Newman, 2004).

Two studies have tested interventions to maintain or improve quality of life and functioning of stem cell transplant patients during the transplant phase. Hayes, Davies, Parker, Bashford, and Newman (2004) found a statistically but not clinically significant decline in the quality of life of patients who underwent stem cell transplant as measured by the CARES questionnaire ($p < 0.05$). With a mixed type, moderate-intensity exercise program, Hayes and co-workers also assessed peak aerobic capacity using a maximal graded treadmill test, pretransplant, posttransplant, and after a 12-week intervention period. The improvement paralleled the overall recovery of the patients' health status because the control group's quality of life also improved during this period ($p < 0.01$). However, at the final measurement point, a clear advantage for the experimental group emerged ($p < 0.05$). Wilson et al. (2005), with their home-based intervention, also showed significant improvements in the quality of life in the experimental group. On the SF-36 health survey, the subscales of "physical function" and "role physical" improvements were noted.

A few studies examined the effects of exercise programs on the quality of life of HSCT patients after transplantation. In Courneya, Mackey, and McKenzie's (2000) study, the focus was on the effects of exercise on the quality of life of cancer patients after transplantation. Baumann, Kraut, Schule, Bloch, and Fauser (2010) found that exposure to an exercise program twice a day during the hospitalization phase could lead to significant positive changes in the overall well-being of HSCT patients. DeFor et al. (2007) focused the effects of a walking regimen on allogeneic transplant patients.

In the DeFor et al. (2007) study about the effects of a walking regimen on allogeneic transplant patients, the results showed improvements in the overall function for all 100 participants in their walking intervention. This was measured using the Karnovsky Scale. For the participants who received a nonmyeloablative regimen, which typically is less intensive, the benefits of the exercise intervention continued through 100 days after the transplantation ($p < 0.01$ and $p = 0.02$).

Courneya, Mackey, and McKenzie (2000) examined the effects of exercise on the quality of life of cancer patients after transplantation. Whereas no specific exercise intervention was utilized, 25 HSCT patients were encouraged to use a bed ergometer in addition to recording the exercise every day. Statistical analysis showed that exercise during hospitalization was significantly correlated with almost all indices of quality of life, including physical well-being, depression, anxiety, and days hospitalized. Some of the correlations were attenuated after controlling for relevant demographic and medical features.

Fatigue and Exercise

Fatigue among cancer patients is a well-recognized phenomenon, affecting almost 90% of cancer patients (Servaes, Verhagen, & Bleijenberg, 2002). This is a concern frequently experienced by HSCT patients as well (Hjermstad et al., 2004). All of the studies reviewed in this section show improvements in the levels of fatigue of HSCT patients, except for one study that did not show significant improvements in the levels of fatigue of HSCT patients (Dimeo, 2001). For the studies that show improvements, exercise was shown to be a factor in decreasing the levels of fatigue of HSCT patients. Individualized exercise programs may be necessary to show improvements among HSCT patients.

Hacker et al. (2006) found that among autologous and allogeneic patients, they experienced reduced activity and increased fatigue for a 5-day period prior to transplant and for 10 days after transplant. The study only followed patients for 10 days posttransplant but did find diminished function, as well as diminished quality of life, and fatigue. Dimeo (2001), in a study with 27 German autologous transplant patients using the Profile of Mood States (POMS) subscale of fatigue, found that the control group had significantly increased levels of fatigue during their hospitalization ($p < 0.05$) whereas the experimental group (training group) had no change in fatigue levels.

There is a sufficient body of evidence that supports the use of exercise to manage fatigue among cancer patients, as well as among HSCT patients. There is a strong body of evidence that supports the use of exercise in the prevention and relief of cancer-related fatigue (Carlson et al., 2006; Kim & Kim, 2005). There remain gaps with regard to issues of theory and approach, which may underlie intervention efficacy.

Of the nonpharmacologic interventions recommended by the National Comprehensive Cancer Network (NCCN) practice guidelines for cancer-related fatigue, exercise has had the strongest evidence base for the treatment of fatigue (Mock et al., 2000). Other interventions that were thought likely to be effective included screening for other etiologies such as depression, thyroid dysfunction, energy conservation and activity management, and relaxation techniques and massage (Jacobsen, Donovan, Vadaparampil, & Small, 2007). Additional research has been recommended to determine the dose, intensity, and frequency of such interventions (Mitchell, Beck, Hood, Moore, & Tanner, 2007).

Several studies have examined forms of exercise interventions among patients who underwent HSCT. Kim and Kim (2006) found that a relaxation breathing exercise along with some passive range of motion done daily for 30 minutes for a 6-week period. They showed greater decreases in the behavioral and cognitive affective subscales on the Piper Fatigue Scale among HSCT patients.

In another study about progressive relaxation, a mixed type exercise program and psycho-education, Jarden, Hovgaard, Boesen, Quist, and Adamsen (2007) examined the effects of progressive relaxation in a sample consisting of 14 allogeneic transplant patients in Denmark. Participants completed a 4- to 6-week program and were evaluated at baseline or pretransplant and on the day of hospital discharge. The intervention group showed improvements in several muscle groups as compared to the control group, which only received conventional care.

Fatigue and the impact of exercise in transplant patients have been examined by multiple researchers. Fatigue has been described as prolonged and intense by many survivors (Gruber, Fegg, Buchman, Kolb, & Hiddemann, 2003; Knobel et al., 2000). Carlson et al. (2006), in a 12-week out-patient intervention with allogeneic patients, reported statistically significant effects for participants on the Fatigue portion of the Functional Assessment of Cancer Therapy (FACT-F) and on the Brief Fatigue Inventory (BFI), showing decreased levels of fatigue. These improvements were almost completely maintained over the 1-year follow-up measurement period. For example, Wilson et al. (2005) demonstrated a decrease in the severity of fatigue related to their aerobic intervention in the home-based setting with patients (mixed allogeneic and autologous), 6 months post transplantation (*p* = 0.05).

Coleman et al. (2003) did not find any significant changes in fatigue among HSCT patients; however, individualized exercise programs may be effective in reducing fatigue among patients who had just undergone multiple myeloma treatment. Their research included multiple myeloma patients undergoing tandem autologous stem cell transplant. The researchers utilized both endurance and resistance training and collected data 3 months prior to the first transplant, at the time of the first transplant, and 3 months after the first transplant.

Physiological Outcomes

The effect of exercise on the overall function of patients is diminished due to the marked heterogeneity of outcomes in many of the studies reviewed (Dimeo et al., 1997; Hayes, Davies, Parker, Bashford, & Green, 2004; Kim & Kim, 2006). Many of these outcomes fall into a category of physiological end points. Some of the results include the effects of exercise interventions on the immune system, changes in body composition, weight, and various psychological traits.

The following studies underscored the positive impact of exercise on a variety of psychosocial parameters, quality of life, function, and physiological outcomes. The majority of these studies utilized endurance types of exercise and did not include resistance training. The only randomized study with resistance training was not completed in the United States and only included autologous patients during the inpatient phase of treatment.

Dimeo et al. (1997), Hayes, Davies, Parker, Bashford, and Green (2004) Hayes, Davies, Parker, Bashford, and Newman (2004), and Kim and Kim (2006) showed that participants that were randomized to an intervention group and also performed daily endurance activity had significant shorter periods of neutropenia ($p < 0.01$). There was also a trend towards a shorter period of thrombocytopenia ($p = 0.06$). Research conducted by Kim and Kim (2006) demonstrated that patients who completed a daily 30-minute bed exercise program for a total of 6 weeks had significant increase in their lymphocyte count ($p = 0.031$). The studies mentioned underscored the possible impact of intervention studies in the immune system.

Several of the studies looked at the changes in the body composition of cancer patients after transplantation. Coleman et al. (2003) found that the intervention group had an increase in weight, whereas the control group lost weight. Weight gain, while not desirable in most populations, may be advantageous in a cancer patient. Hayes, Davies, Parker, Bashford, and Green (2004) demonstrated that a reduced percentage of body fat ($p = 0.04$) in the experimental group leads to an enhancement in the fat-free mass ($p < 0.01$) and a significant increase in total energy expenditure ($p < 0.01$) when compared with the pretreatment group. Cunningham et al. (1986) did not find any significant changes in body composition in their study among allogeneic transplant patients.

Psychological Outcomes

Psychological distress can also have a significant impact on recovery. Symptoms such as depression, anxiety, and anger can add to the on-going challenge of regaining function and strength.

Some of these parameters were assessed by the Profile of Mood States (POMS). Dimeo et al. (1997) demonstrated that a hospital-based endurance program could reduce anger/hostility in the intervention group ($p < 0.01$). The intervention group also had no change in the "vigor" subscale of the POMS, whereas the control group showed significant deterioration in "vigor." In the Carlson et al. (2006) study, improvement in the "vigor" subscale of the POMS in their participants emerged after a 12-week aerobic exercise program ($p < 0.01$). Vigor in these studies presumably was defined as similar to function or performance of daily activity.

A variety of other traits and symptoms have been examined by previous researchers. Dimeo et al. (1997) found that on the symptom check list SCL-90-R (Derogatis, 1974), obsessive-compulsive traits, anxiety, and global psychological distress were reduced with patients who exercised, whereas the participants in the control group exhibited more somatization ($p < 0.01$).

In a study by Andrykowski et al. (2005), 662 survivors of transplant (mean of 7 years post-HSCT) were compared with healthy patients. The HSCT (both allogeneic and autologous) group reported poorer status relative to the healthy comparison group, after matching for age and gender, on physical function, physical health, and social functioning. However, the survivors reported more psychological and interpersonal growth.

Physical limitations, return to work, depression, and distress related to treatment or disease were evaluated before transplantation, after 90 days, and at 1, 3, and 5 years after HSCT. Syrjala et al. (2004) examined 319 patients who received either an autologous or allogeneic transplant for leukemia or lymphoma. The researchers found that recovery occurred gradually over 1-5 years as measured by improvement in physical function, return to work, depression, and treatment related distress. Whereas physical recovery occurred earlier than work or psychological recovery, only 19% of patients recovered on all outcomes at 1 year posttransplant. Transplant related distress was slower to recover for allogeneic transplant patients and those with less social supports prior to transplant ($p < .01$).

In a recent study by DeFor et al. (2007), the effects of exercise intervention were examined before, during, after HSCT among allogeneic patients. The results indicated improvement in all time points in terms of the reduction of fatigue, improvement in physical fitness, and decrease in global distress. DeFor et al. recommended a supervised exercise program to be integrated into the recovery of HSCT allogeneic patients.

Recommendations for the integration of exercise are important first steps to improving supportive care for HSCT patients. There are many questions still to be answered prior to integration in to practice. The optimal type and dose of exercise, barriers to implementation, and the need for long-term follow-up all remain key areas for future research.

Types of Exercise

The most common type of exercise intervention utilized with HSCT patients is endurance/aerobic, which is typically assessed by previous researchers using stationary bicycle or treadmill. Patients appeared to benefit from aerobic exercise regardless of whether it was done in an in-patient, out-patient, or home-based setting (Carlson et al., 2006; Dimeo et al., 1997; Hayes, Davies, Parker, Bashford, & Green, 2004).

The study conducted by Dimeo et al. (1997) showed that regular endurance training may not lead to an actual increase in endurance performance; however, the researchers found that the loss of performance in the intervention groups was significantly lower than in the control groups ($p < 0.05$). This may point to the possibility that exercise may serve to stabilize the physical status of patients as opposed to improving their status. An increase in physical performance with endurance training could not be shown during in-patient hospitalization in another uncontrolled study (Dimeo et al., 2003). There were no significant decreases reported at the time of hospital discharge or during the in-patient period.

Aerobic interventions that carried over from in-patient to out-patient care had better endurance levels, pre- and postintervention ($p < 0.01$; Carlson et al., 2006; Hayes, Davies, Parker, Bashford, & Green, 2004).

A home based study by Wilson et al. (2005) utilized aerobic activity, which was unsupervised by the research team, showed positive effects in endurance performance ($p < 0.05$). Two other home based studies demonstrated no statistically significant differences in aerobic performance (Coleman, 2003; Decker, Turner-McGlade, & Fehir, 1989).

Hayes, Davies, Parker, Bashford, and Green (2004), Hayes, Davies, Parker, Bashford, and Newman (2004), and Mello et al. (2003) found that resistance exercise provided benefits for patients in a primarily out-patient setting. Hayes and co-workers found significant increases in the intervention group in upper body strength. In Mello et al.'s (2003) study, the researchers used a combined in and out patient intervention. They found a stabilization effect of the resistance training regarding different extremities muscle groups in the intervention group. At the same time, the strength testing in the control group decreased ($p < 0.01$).

Aerobic/endurance exercise was the most commonly utilized exercise in many interventions. Few researchers used the combination of resistance training and endurance activity. Only three of the studies reviewed used this combination. Some used a combination of endurance with relaxation, stretching, and psycho-education. Of these two, only one was a randomized trial and both were completed outside the United States. One utilized autologous patients, whereas the other included only allogeneic participants.

From this review, endurance training had a stabilization effect during transplant while it had an improving effect after transplant. Strength training showed similar results. Because of the variety of definitions of during and after transplant these results should be cautiously considered. Resistance training is an important component of any training program among healthy persons (Lucia, Earnest, & Perez, 2003) and is recommended along with endurance training by the American College of Sports Medicine ([ACSM], 2006). In a review of 26 exercise intervention studies with cancer patients by Galvao and Newton (2005), the use of resistance training during cancer treatment as an exercise mode to counteract side effects was supported. The use of endurance and resistance training was further supported by the work of Schneider, Hsieh, Sprod, Carter, and Hayward (2007) and Dimeo, Schwartz, Wesel, Voigt, and Thiel (2008).

Schmitz et al. (2010) examined previous studies regarding the effects of exercise during and after HSCT. The results of their examination indicated that exercise is a safe practice during and after HSCT. Aerobic and muscular strength exercises have been shown to be effective in improving the overall fitness of HSCT patients, including their quality of life, reduction of fatigue, and improvement of immune system.

Shelton et al. (2008) examined whether there were differences in results among allogeneic patients based on the two types of exercise programs. The results showed that either program was beneficial and no significant difference existed between self-directed and supervised exercise programs. Shelton et al. concluded that short-term exercise programs were beneficial to allogeneic patients regardless of how the exercise program was implemented.

Exercise Recommendations

No specific exercise recommendations for HSCT patients have been developed by previous researchers. The majority of the studies reviewed utilized endurance exercise, such as walking on a treadmill or cycling on a stationary bicycle for 30 minutes, which is the standard length of time recommended by the American College of Sports Medicine. Several studies utilized both resistance and endurance with none offering progressive interventions. Most were individualized for the participant's abilities. No specific exercise recommendations for HSCT patients in terms of frequency, duration, intensity, type, and progression were explored and examined by previous researchers.

The ACSM recommended that an exercise prescription consist of five components: (a) frequency, (b) duration, (c) intensity, (d) type, and (e) progression. Frequency is the number of sessions per week; intensity is how hard the person is exercising; type is the mode of exercise; time is the duration of each activity session; and progression is how frequency, intensity, and duration are increased over time. These parameters have rarely been addressed in exercise research with cancer patients or HSCT patients.

Courneya, Vallance, Jones, and Reiman (2005) made suggestions for prescribing aerobic exercise with cancer patients and these have been referenced by others (Schneider, Dennehy, & Carter, 2003). After reviewing the literature on aerobic exercise among cancer patients, Courneya, Mackey, and Jones (2000) suggested that for cancer patients, large muscle groups can be stimulated through walking or bicycling. The researchers also recommended that the frequency of the exercise should be three to five times weekly, adding that daily activity was optimal. Intensity should be moderate, approximately 50-75% of maximal heart rate reserve with a duration of 20-30 minutes and progression should be increased in frequency and duration.

The recommendations for relatively healthy cancer survivors and early stage patients with cancer were more conservative. The review conducted suggested that no available published guidelines for resistance or endurance exercise programs for patients with cancer or recovering from cancer exists. The ACSM recommended that healthy individuals exercise 3-5 days every week. In a de-conditioned population, shorter exercise sessions per day are more appropriate. The ASCM further suggested healthy individuals to take 2-3 nonconsecutive days per week of resistance training. The days should be nonconsecutive to allow the muscles time to repair between resistance exercise sessions.

Intensity typically has two main components: (a) measuring or predicting the maximum intensity the individual can tolerate, and (b) measuring or calculating an individual's target intensity range. The typical method of predicting maximum intensity is through the calculation of Age Predicted Maximum Heart Rate (APMHR) by subtracting the age of a person from 220. Using the APMHR, the individual's target intensity range, or target heart range, can be calculated using the heart rate reserve method known as the Karvonen method. This method calculates a percentage of heart rate reserve, wherein percentages vary depending on the individual. The ACSM recommended a heart rate reserve intensity between 40% and 85% for the relatively healthy population; however, beta-blocker medications can invalidate this formula. For the relatively healthy patients, perceived exertion can be a means of gauging intensity, which can be used to prescribe the intensity of the exercise.

The most commonly used perceived exertion scale is the Borg Scale (Borg, 1998). While there are several versions, the most common version ranges from 6-20. The numbers are intended to correlate with the heart rate of healthy individuals (Borg, 1998). Patient's report of perceived exertion did not appear to be influenced by medications that affect the heart. Individuals should aim to exercise at an intensity between 12 and 16 (which can be qualitatively referred to as somewhat hard to hard; ASCM, 2006). Courneya, Mackey, and Jones (2000) recommended that cancer patients exercise at a level of 50-75% of maximum heart rate and at a perceived exertion of 13-15. The ACSM recommended that aerobic exercise for sedentary low risk individuals last for about 15-30 minutes per session, with flexibility training doing each stretch two to four times, holding the stretch for 15-30 seconds. Progression, according to the ACSM, will depend on multiple factors such as fluctuating blood counts, symptoms such as fatigue and nausea, and infection.

There may be instances wherein exercise is contraindicated. The symptoms in patients undergoing a stem cell transplant are unpredictable; thus, these patients may not progress but maintain a certain level of fitness. If progress is achieved, the trajectory is likely to be nonlinear (Wiskemann & Huber, 2008).

Whereas the ACSM has published guidelines for patients with various clinical conditions, such as obesity, osteoporosis, pulmonary disease, and peripheral artery disease, very little is known about the parameters for patients undergoing treatments for cancer or stem cell transplant. There remain no clear guidelines for exercise prescription for HSCT patients. It is clear that interventions do need to be individualized knowing that no two patients will have the same requirements. Participants will vary in their pulmonary, cardiovascular, and muscle strength, as well as their exercise history and level of motivation. An individualized exercise program that responds to physical and psychological changes that patients go through as they undergo treatment is also essential to keep the participants involved at a level that is appropriate (Schneider, Dennehy, Roozeboom, & Carter, 2002).

Barriers to Exercise

Adherence to an exercise program is essential for continued improvement and stabilization of physical status. None of the studies reviewed looked at long-term follow-up beyond 100 days status posttransplant. Adherence in the hospital based interventions was superior to that of the home based interventions because of the direct supervision received by the patients. The Coleman et al. study (2003) was the only study that examined barriers and included factors that would enhance patients' adherence to a prescribed exercise program. Future studies examining the therapeutic sustainability of applied interventions are important because questions regarding adherence, lifestyle change, and understanding factors that contribute to compliance with exercise are relevant.

A number of variables have been identified that may influence levels of physical activity. Some of these variables are demographics, cognition, social environments, and physical environment (Buckworth & Dishman, 1999). Cognitive variables are generally targeted because they are more amenable to change. Perceived benefits and perceived barriers are often cited as accounting for levels of physical exercise (Brown, 2005). These variables are included in several health belief models such as the health belief model and the model of planned behavior (Ajzen & Driver, 1992). Other barriers often cited are lack of time and/or opportunity, fatigue, poor self-image, and lack of desire (Brown, 2005).

Primary barriers to exercise among HSCT patients include nausea, lack of strength, lack of desire, and lack of energy. In one of the larger studies conducted by Defor et al. (2007), the researchers found that only 24% of patients on the exercise arm followed the suggested routine 100 % of the time. Of the 24 studies reviewed, compliance with the intervention was approximately 70%; however, the two home-based studies (Defor et al., 2007; Wilson et al., 2005) had 65% compliance, which could be attributed to a lack of direct supervision.

Summary of Studies Reviewed

For pretransplant status, the studies of White et al. (2005) and Kebriaei et al. (2005) indicated that prior to transplant, HSCT patients have poor health status. The poor status may manifest in terms of respiratory and muscle strength. Table 3 contains a summary of the major studies reviewed on pretransplant status.

After transplantation, fatigue is experienced by HCST patients, for both autologous and allogeneic (Hacker et al., 2006). Fatigue for both autologous and allogeneic patients can be alleviated through exposure to exercise intervention programs (Carlson et al., 2006; Jarden et al., 2007; Wilson et al., 2005). Exercises such as relaxation breathing exercise and some passive range of motion have been effective in decreasing fatigue among HSCT patients (Kim & Kim, 2005).

Table 4 contains a summary of the major studies reviewed with regard to fatigue among HSCT patients.

Studies on quality of life after transplantation showed that there was correlation between quality of life and exercise during hospitalization (Courneya, Mackey, & Jones, 2000). In the Baumann et al. study (2010), exposure to exercise during the early phase of the treatment, such as during hospitalization, could improve the general quality of life of HSCT patients. Aerobic capacity was also correlated with quality of life among transplant patients (Hayes, Davies, Parker, Bashford, & Newman, 2004).

Table 5 contains a summary of the major studies reviewed on the section, quality of life.

Based on the two major studies reviewed (Andrykowski et al., 2005; Syrjala et al., 2004), there is research evidence that after transplant, the well-being of HSCT patients tends to deteriorate physically, emotionally, socially, and psychologically (Andrykowski et al., 2005). Full recovery is only expected to be achieved 3-4 years after the transplantation (Syrjala et al., 2004).

Table 6 contains a summary of the major studies reviewed for the section on physiological/psychological outcomes.

Most studies on the types of exercise that HSCT, patients were exposed to endurance and aerobic exercise for in-patient, out-patient, and home-based settings (Carlson et al., 2006; Decker et al., 1989; Dimeo et al., 1997, 2003; Hayes, Davies, Parker, Bashford, & Green, 2004). Resistance training was primarily used by out-patients (Galvao & Newton, 2005; Hayes, Davies, Parker, Bashford, & Green, 2004; Mello et al., 2003). Research on the combination of endurance and resistance was lacking, but the general belief is that the combination is beneficial for both healthy and cancer patients (ACSM, 2006; Dimeo et al., 2008; Lucia et al., 2003; Schneider et al., 2007).

Table 7 contains a summary of the major studies on types of exercise.

Specific exercise recommendations for HSCT patients in terms of frequency, duration, intensity, type, and progression, were lacking. Schmitz et al. (2010) examined the effects of exercise during and after HSCT based on a review of previous studies; however, no specific exercise recommendations were reported.

Table 8 contains a summary of exercise recommendations for cancer patients, both for relatively healthy and sedentary cancer patients.

Discussion

The majority of the studies reviewed show a positive impact of exercise on physiological and psychological aspects of recovery from HSCT. There are a number of limitations to this review. First, there was a diversity of exercise intervention types across the various studies. Second, the timing of studies varied across the trajectory of transplant from during actual hospitalization and chemotherapy to all the way up to a year post transplant. Both of these limitations might be expected to result in different outcomes. There remains no consensus as to the type or dose of activity that is optimal. Most studies often combined the allogeneic and autologous transplant types, possibly skewing the outcomes of studies despite enhancing generalizability. Moreover, a variety of disease groups, ages, and settings were utilized. Many of the trials to date were nonrandomized with small sample sizes (12-100/average 40 participants) with high attrition rates. Participants were often not from the United States, limiting the generalizability. Only one study, Jones et al. (2006), used a theoretical framework to examine the impact of exercise programs on HSCT patients. Use of a theoretical framework may lay the groundwork for the development of interventions aimed at enhancing adherence to exercise behavior.

Despite the general findings among researchers that exercise programs can be beneficial to the recovery of HSCT patients, the nature of the appropriate exercises is not clear (Wiskemann & Huber, 2008). There remain no clear guidelines for exercise prescription for HSCT patients (Courneya, Mackey, & Jones, 2000). Related areas of research include the examination of the impact of exercise on psychological stress during HSCT and the development of interventions to facilitate adherence to exercise behaviors.

Significant benefits from exercise interventions in stem cell transplantation have been consistently reported for physical performance/function, fatigue, and quality of life. Research is needed to provide more rigorous examinations of these interventions to address methodological problems such as small sample size, diversity of settings, and lack of theoretical framework. Validating the positive results from previous study in this area for the purpose of evidence-based practice is paramount to improving the quality of care post transplantation.

Table 3

Summary of Major Studies for Pretransplant Status

Study	Design	Setting/Sample	Measures	Results
White, Miller, and Ryan (2005)	Quanti-Observational	Boston, Massachusetts/ *N* = 56 (HSCT-allogeneic)	PFT PImax PEmax GS 6MWT	Respiratory and skeletal muscle strength and maximal exercise capacity are reduced in a substantial percentage of patients prior to allogeneic transplant.
Kebriaei, Kline, Kasza, Le Beau, Larson, and Van Besien (2005)	Quanti (retrospective series)	Chicago, Illinois/ N = 68 (SCT-allogeneic)	Eastern Cooperative Oncology Groups performance scale	Pretransplant disease burden and poor outcome after SCT are correlated.

Table 4

Summary of Major Studies on Fatigue

	Design	Setting/Sample	Measures	Results
Carlson, Smith, Russell, Fibish, and Whittaker (2006)	Quanti (time series)	(N = 12)/ allogeneic patients	Functional Assessment of Cancer Therapy (FACT-F) and on the Brief Fatigue Inventory (BFI)	Twelve-week out-patient individualized exercise program was effective in decreasing levels of fatigue among allogeneic patients, which were able to be maintained for a year.
Coleman, Coon, Hall-Barrow, Richards, Gaylor, and Stewart (2003)	Quanti (feasibility study)	(N = 24)/ autologous stem cell transplant patients	Endurance and resistance training	Among cancer patients, no significant changes in fatigue occurred as a result of exercise; however, individual-ized exercise programs may be effective in reducing fatigue among patients who had just undergone multiple myeloma treatment.
Hacker, Ferrans, Verlen, Ravandi, Van Besien, Gelms, and Dieterle (2006)	Quanti (prospective)	Midwest (N = 20)/ autologous and allogeneic HSCT	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, Quality of Life Index	The results indicated that after high-dose chemotherapy and HSCT treatments for both allogeneic and autologous patients, fatigue significantly increases. The nature of the fatigue experienced can be physical, emotional, and cognitive.

Table 4 (continued)

	Design	Sample-setting	Measures	Results
Kim and Kim (2005)	Quanti-Randomized	Korea (N=35) Allogeneic	Piper Fatigue Scale	Relaxation breathing exercise and some passive range of motion done daily for 30 minutes- 6 week period showed greatest decreases in behavioral and cognitive affective components of fatigue among allo patients

Table 5

Summary of Major Studies on Quality of Life

Study	Design	Setting/ Sample	Measures	Results
Baumann, Kraut, Schule, Block, and Fauser (2010)	Quanti (random)	(N = 64)/ inpatient allogeneic and autologous HSCT	Controlled trials	The results showed that exposure to exercise program twice a day during the hospitalization phase could lead to significant positive changes in the overall well-being of HSCT patients.
Dimeo, Fetscher, Lnaage, Mertelsmann, and Keul (1997)	Quanti	(N = 33)/ HSCT patients	Bed ergometer, self-report	Exercise during hospitalization significantly correlated with almost all indices of quality of life, including physical well-being, depression, anxiety, and number of days hospitalized.
Defor, Burns, Gold, and Weisdorf (2007)	Quanti (randomized trial)	(N = 100)/ allogeniec transplant patients	Karnofsky score (KPS)	Allogeneic transplant patients who participated in a walking exercise showed improvements in physical and emotional well-being. A less-intensive version of the walking exercise program showed similar improvements 100 days after transplantation.

Table 5 (continued)

Study	Design	Setting/ Sample	Measures	Results
Hayes, Davies, Parker, Bashford, and Newman (2004)	Quanti (evaluative)	(N = 12)/ stem cell transplant patients	CARES questionnaire and peak aerobic capacity by a maximal graded treadmill test	A statistically but not clinically significant decline in the quality of life of patients who underwent stem cell transplant was observed after exposure to exercise. Peak aerobic capacity and quality of life were also found to be correlated

Table 6

Summary of Physiological/Psychological Outcomes

Study	Design	Setting/Sample	Measures	Results
Andrykowski, Bishop, Hahn, Cella, Beaumont, Brady . . . Wingard (2005)	Quanti (comparative)	(N = 662)/ HSCT survivors	Standardized measures of HRQOL and growth and spiritual well-being	Results indicated that HSCT patients had significantly lower functioning in terms of physical, psychological, and social well-being compared to non-HSCT patients. Psychological and interpersonal growth was observed from HSCT patients.
Syrjala, Langer, Abrams, Storer, Sanders, Flowers, and Martin (2004)	Quanti (prospective longitudinal cohort study)	(N = 99)/HCT survivors, autologous/ allogeneic	Physical function, return to work, depression, and treatment related distress	Physical recovery occurs earlier among HCT survivors compared to work and psychological recovery. At the first year after the transplant, only 21% achieved full recovery. Full recovery usually occurs 3-4 years after the transplantation.

Table 7

Summary of Major Studies on Types of Exercise

Type of Exercise	Sources	Settings	Results
Endurance/ aerobic	Carlson, Smith, Russell, Fibish, and Whittaker (2006); Decker, Turner-McGlade, and Fehir (1989); Dimeo, Fetscher, Lnaage, Mertelsmann, and Keul (1997); Dimeo, Schwartz, Fietz, Wanjura, Boning, and Thiel (2003); Hayes, Davies, Parker, Bashford, and Green (2004)	In-patient, out-patient, or home-based	Stabilization during transplant, but not necessarily improvement among HSCT patients. Improvement occurs after transplant
Resistance	Galvao & Newton (2005); Hayes, Davies, Parker, Bashford, and Green (2004); Mello, Tanaka, and Dulley (2003)	Primarily outpatients	Significant increases in body strength. The use of resistance training during cancer treatment as an exercise mode to counteract side effects is supported.
Endurance + resistance	(ACSM, 2006; Dimeo, Schwartz, Wesel, Voigt, and Thiel (2008); Lucia, Earnest, and Perez (2003); Schneider, Hsieh, Sprod, Carter, and Hayward (2007)	Healthy patients and cancer patients	The combination of both exercises is beneficial for both healthy and cancer patients.

Table 8

Summary of Major Studies on Exercise Recommendations

Type of Patients	Frequency	Duration	Intensity	Type	Progression
Cancer patients (Courneya, Mackey, & Jones, 2000)	3-5 times a week	20-30 minutes	Moderate	Walking/bicycling	Increases in frequency and duration
Relatively healthy cancer survivors (ACSM, 2006)	3-5 days every week		40-85% APMHR	Resistance training	
Sedentary (ACSM, 2006)	2-4 times a week	5-30 minutes		Flexibility	Dependent on various factors
HSCT	No data	No data	No data	No data	No data

References

Ajzen, I., & Driver, B. L. (1992). Application of planned behavior to leisure choice. *Journal of Leisure and Rest, 24*(3), 207-224.

American College of Sports Medicine. (2006). *ACSM's guidelines for exercise testing and prescription* (7th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Andrykowski, M. A., Bishop, M. M., Hahn, E. A., Cella, D. F., Beaumont, J. L., Brady, M. J., . . . Wingard, J. R. (2005). Long-term health related quality of life, growth and spiritual well-being after hematopoietic stem-cell transplantation. *Journal of Clinical Oncology, 23*(3), 599-608.

Baumann, F. T., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation*, *45,* 355-362.

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker S., Gurney, J. G., . . . Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: Report from the Bone Marrow Transplant Survivor Study. *Blood, 110*(10), 3787-3792.

Borg, G. (1998). *Borg's perceived exertion and pain*. Champaign, IL: Human Kinetics.

Brown, S. A. (2005). Measuring perceived benefits and perceived barriers for physical activity. *American Journal of Health Behavior, 29*(2), 107-116.

Buckworth, J., & Dishman, R. K. (1999). *Determinants of physical activity: Research to application.* Malden, MA: Blackwell Science.

Carlson, L. E., Smith, D., Russell, J., Fibich, C., & Whittaker, T. (2006). Individualized exercise program for the treatment of severe fatigue in patients after allogeneic hematopoietic stem-cell transplant: A pilot study. *Bone Marrow Transplantation, 37,* 945–954.

Coleman, E., Coon, S., Hall-Barrow, J., Richards, K., Gaylor, D., & Stewart, B. (2003). Feasibility of exercise during treatment for multiple myeloma. *Cancer Nursing, 26,* 410-419.

Courneya, K., & Friedenreich, C. M. (1997). Determinants of exercise during colorectal cancer treatment: An application of the theory of planned behavior. *Oncology Nursing Forum, 24*(10), 1715-1723.

Courneya, K., & Friedenreich, C.M. (1999). Utility of the theory of planned behavior for understanding exercise during breast cancer treatment. *Psychooncology, 8*, 112-122.

Courneya, K., Friedenreich, C. M., Arthue, K., & Bobick, T. M. (1999). Understanding exercise motivation in colorectal patients: A prospective study using the theory of planned behavior. *Rehabilitation Psychology, 44*(1), 68-84.

Courneya, K., Friedenreich, C. M., Sela, R. A., Quinney, H. A., & Rhodes, R. E. (2002). Correlates of adherence and contamination in a randomized controlled trial of exercise in cancer survivors: An application of the theory of planned behavior and the five factor model of personality. *Annals of Behavioral Medicine, 24*, 257-268.

Courneya, K., Keats, M. R., & Turner, A. R. (2000). Social cognitive determinants of hospital-based exercise in cancer patients following high dose chemotherapy and bone marrow transplantation. *International Journal of Behavioral Medicine, 7*(3), 189-203.

Courneya, K., Mackey, J. R., & Jones, L. W. (2000). Coping with cancer: Can exercise help? *Physical Sports Medicine, 28*, 49-73.

Courneya, K., Mackey, J. R., & McKenzie, D. C. (2000). Physical exercise and quality of life in cancer patients following high dose chemotherapy and autologous bone marrow transplantation. *Psycho-oncology, 9*, 127-136.

Courneya, K., Vallance, J. K. H., Jones, L. W., & Reiman, T. (2005) Correlates of exercise intentions in non-Hodgkin's lymphoma survivors: An application of the theory of planned behavior. *Journal of Sports Medicine Psychology, 27*, 335-347.

Cunningham, B., Morris, G., Cheney, C. L., Buergel, N., Aker, S. N., & Lenssen, P. (1986). Effects of resistive exercise on skeletal muscle in marrow transplant recipients receiving total parental nutrition. *Journal of Parenteral Enteral Nutrition, 10*, 558-563.

Decker, W., Turner-McGlade, J., & Fehir, K. M. (1989). Psychological aspects and the physiological effects of a cardiopulmonary exercise program in patients undergoing bone marrow transplantation (BMT) for Acute Leukemia (AL). *Transplant Proceedings, 21*(1, Pt. 3), 3068-3069.

Defor, T., Burns, L. J., Gold, E. M., & Weisdorf, D. J. (2007). A randomized trial of the effect of a walking regimen on the functional status of 100 adult allogeneic donor hematopoietic cell transplant patients. *Biology of Blood and Marrow Transplant, 13*(8), 948-955.

Demark-Wahnefried, W., Morey, M. C., Clipp, E. C., Pieper, C. F., Snyder, D. C., Sloane, R., & Cohen, H. J. (2003). Leading the Way in Exercise and Diet (Project LEAD): Intervening to improve function among older breast and prostate cancer survivors. *Controlled Clinical Trials, 24*(2), 206-223.

Derogatis, L. R. (1974). The Hopkins Symptom Checklist. In P. Pichot (Ed.), *Psychological measurements in psychopharmacology* (pp. 79-111). Oxford, England: Karger.

Dimeo, F. (2001). Effects of exercise on cancer-related fatigue. *Cancer, 92*(6), 1689-1693.

Dimeo, F., Fetscher, S., Lnaage, W., Mertelsmann, R., & Keul, J. (1997). Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood, 90*, 3390-3394.

Dimeo, F., Schwartz, S., Fietz, T., Wanjura, T., Boning, D., & Thiel, E. (2003). Effects of endurance training on the physical performance of patients with hematological malignancies during chemotherapy. *Supportive Care Cancer, 1,* 623-628.

Dimeo, F., Schwartz, S., Wesel, N., Voigt, A., & Thiel, E. (2008). Effects of endurance and resistance exercise program on persistent cancer-related fatigue after treatment. *Annals of Oncology, 19*(8), 1495-1499.

Galvao, D. A., & Newton, R. U. (2005). Review of exercise interventions: Studies in cancer patients. *Journal of Clinical Oncology, 23*(4), 899-909.

Gratwohl, A., Baldomero, H., Aljurf, M., Pasquini, M. C., Bouzas, L. F., Yoshimi, A., . . . Kodera, Y. (2010). Hematopoietic stem cell transplantation: A global perspective. *Journal of the American Medical Association, 303*(16, 1617-1624.

Gruber, U., Fegg, M., Buchman, M., Kolb, H. F., & Hiddemann, W. (2003). The long-term psychosocial effects of haematopoietic stem cell transplantation. *European Journal of Cancer Care, 12*, 249-256.

Hacker, E., Ferrans, C., Verlen, E., Ravandi, F., Van Besien, K., Gelms, J., & Dieterle, N. (2006). Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncology Nursing Forum, 33*(3), 614-624.

Hayes, S., Davies, P. S., Parker, T., Bashford, J., & Green, A. (2004). Role of a mixed-type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *British Journal of Sports Medicine, 38,* 304-309.

Hayes, S., Davies, P. S. W., Parker, T., Bashford, J., & Newman, B. (2004). Quality of life changes following peripheral blood stem cell transplantation and participation in a mixed-type, moderate-intensity, exercise program. *Bone Marrow Transplantation, 33,* 553–558. doi:10.1038/sj.bmt.1704378

Hjermstad, M. J., Knobel, H., Brinch, L., Fayers P. M., Loge J. H., Holte H., & Kaasa, S. (2004). A prospective study on health-related quality of life, fatigue, anxiety and depression 3-5 years after stem cell transplantation. *Bone Marrow Transplant, 34*, 257-266.

Illman, A., Stiller, K., & Williams, M. (2000). The prevalence of orthostatic hypotension during physiotherapy treatment with patients with an acute spinal cord injury. *Spinal Cord*, *38*, 741-747.

Jacobsen, P. B., Donovan, K. A., Vadaparampil, S. T., & Small, B. J. (2007). Systematic review and meta-analysis of psychological and activity-based interventions for cancer related fatigue. *Health Psychology*, *26*(6), 660-667.

Jarden, M., Hovgaard, D., Boesen, E., Quist, M., & Adamsen, L. (2007). Pilot study of a multimodal intervention: Mixed-type exercise and psychoeducation in patients undergoing allogeneic stem cell transplantation. *Bone Marrow Transplantation, 40*, 793-800.

Jones, L., Courneya, K. S., Vallanec, J. K., Ladha, A. B., Mant, M. J., Belch, A. R., & Reiman, T. (2006). Understanding the determinants of exercise intentions in Multiple Myeloma. *Cancer Nursing*, *29*(3), 167-175.

Kebriaei, P., Kline, J., Kasza, K., Le Beau, M. M., Larson, R. A., & van Besien, K. (2005). Impact of disease burden at time of allogeneic stem cell transplantation in adults with acute myeloid leukemia and myelodysplastic syndromes. *Bone Marrow Transplantation*, *35*, 965-970.

Kim, S., & Kim, H. S. (2005). Effects of a relaxation breathing exercise on fatigue in haemopoietic stem cell transplantation patients. *Journal of Clinical Nursing, 4*(1), 51–55. doi: 10.1111/j.1365-2702.2004.00938.x

Kim, S., & Kim, H. S. (2006). A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. *European Journal of Cancer Care—English Version*, *15*, 453-457.

Knobel, H., Loge, J. H., Nordoy, T., Kolstad, A. L., Espevik, T., Kvaloy, S., & Kaasa, S. (2000). High level of fatigue in lymphoma patients treated with high dose therapy. *Journal of Pain and Symptom Management*, *19*, 446-456.

Lucia, A., Earnest, C., & Perez, M. (2003). Cancer-related fatigue: Can exercise physiology assist oncologists? *Lancet Oncology, 4,* 616-625.

Mello, M., Tanaka, C., & Dulley, F. L. (2003). Effects of an exercise program on muscle performance in patients undergoing allogeneic bone marrow transplantation. *Bone Marrow Transplant, 32,* 723-728.

Mitchell, S., Beck, S. L., Hood, L. E., Moore, K., & Tanner, E. R. (2007). Putting evidence in to practice: Evidence-based interventions for fatigue during and following cancer and its treatments. *Clinical Journal of Oncology Nursing, 11*(1), 99-113.

Mock, V., Atkinson, A., Barsevick, A., Cella, D., Cimprich, B., Cleeland, C., . . . Stahl, C. (2000). NCCN practice guidelines for cancer-related fatigue. *Oncology, 14,* 151-161.

Morishita, S., Kaida K., Tanaka, T., Itani, Y., Ikegame, K., Okada, M., . . . Domen, K. (2012). Impaired physiological function and health-related QOL in patients before hematopoietic stem-cell transplantation. *Support Care in Cancer, 20*(4), 821-829.

Rovo, A., Daikeler, T., Stern, M., Halter, J., Studt, J. D., Buser, A., . . . Tichelli, A. (2008). Physical and not mental health is impaired in very long term survivors after HSCT compared with their respective donors: A paired analysis. *Blood, 111*(3), 1740-73`.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1996). Allogeneic blood cell transplants for haematological malignancy: Preliminary comparison of outcomes with bone marrow transplantation. *Bone Marrow Transplant, 17,* 703-708.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1997). Second allogeneic transplants for leukemia using blood instead of bone marrow as a source of hematopoietic cells. *Bone Marrow Transplant, 18,* 501-505.

Russell, J. A., Desai, S., Herbut, B., Brown, C., Luider, J., Ruether, J. D., . . . Klassen, J. (1997). Partially mismatched blood cell transplants for high-risk hematologic malignancy. *Bone Marrow Transplant, 19,* 861-866.

Russell, J. A., Larratt, L., Brown, C., Turner, A. R., Chaudhry, A., Booth, K., . . . Poon, M. C. (1999). Allogeneic blood stem cell and bone marrow transplantation for acute myelogenous leukemia and myelodysplasia: Influence of stem cell source on outcome. *Bone Marrow Transplant, 24,* 1177-1183.

Schmitz, K., Courneya, K., Mathews, C., Demark-Wahnefried, W., Galvao, D., Pinto, B., . . . Schwartz, A. (2010). American College of Sports Medicine roundtable on exercise guidelines for cancer survivors, *Medicine & Science in Sports and Exercise, 43*(1), 1409-1425.

Schneider, C., Dennehy, C. A., & Carter, S. D. (2003). *Exercise and cancer recovery*. Champaign, IL: Human Kinetics.

Schneider, C., Dennehy, C. A., Roozeboom, M., & Carter, S. D. (2002). Prescriptive exercise rehabilitation adaptations in cancer patients. *Medical Science of Sports Exercise*, *32*(5), S234.

Schneider, C., Hsieh, C. C., Sprod, L. K., Carter, S. D., & Hayward, R. (2007). Cancer treatment-induced alterations in muscular fitness and quality of life: The role of exercise training. *Annals of Oncology, 18*(12), 1957-1962.

Servaes, P., Verhagen C., & Bleijenberg G. (2002) Fatigue in cancer patients during and after treatment: Prevalence, correlates and interventions. *European Journal Cancer, 38,* 27-43.

Shelton, M. L., Lee, J. Q., Morris, G. S., Massey, P. R., Kendall, D. G., Munsell, M. F., . . . Giralt, S. A. (2009). A randomized control trial of a supervised versus a self-directed exercise program for allogeneic stem cell transplant patients. *Psycho-oncology, 18,* 353-359.

Sullivan, K M. (1999). Graft versus host disease. In S. J. Forman, K. G. Blume, & E. D. Thomas (Eds.), *Hematopoietic stem cell transplantation* (pp. 515-536). Boston, MA: Blackwell Science.

Syrjala, K., Langer, S. L., Abrams, J. R., Storer, B., Sanders, J. E., Flowers, J. E., & Martin, P. J. (2004). Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. *Journal of the American Medical Association*, *291*(19), 2335-2343.

White, A., Miller, K. B., & Ryan, H. F. (2005). Impaired respiratory and skeletal muscle strength in patients prior to hematopoietic stem cell transplantation. *Chest, 128*, 145-152.

Willenbacker, W., Mumm, A., Ruither A., Weis, J., & Bartsch, H. (1998). Somatic risk factors for intermediate and long-term sequelae after hematological stem cell therapy: Predictive for feasibility of a rehabilitation program. *Oncology,* 21, 217-223.

Wilson, R., Jacobsen, P. B., & Fields, K. K. (2005). Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. *Bone Marrow Transplant*, *35*, 721-727.

Wiskemann, J., & Huber, G. (2008). Physical exercise as adjuvant therapy for patients undergoing hemtopoietic stem cell transplantation. *Bone Marrow Transplant*, *41*, 321-329.

CHAPTER 3

THE IMPACT OF EXERCISE ON ALLOGENEIC AND AUTOLOGOUS STEM CELL PATIENTS DURING ACTIVE TREATMENT

Randi Hoffmann, RN, PhD (c)
Mayo Clinic, Rochester, Minnesota

Kathi Mooney, RN, PhD, FAAN
University of Utah—College of Nursing

Debra Barton, RN, PhD, AOCN, FAAN
Mayo Clinic, Rochester, Minnesota

Erin Rothwell, PhD, TRS, CTRS, CRSS
University of Utah—College of Nursing

Paul C. LaStayo, PT, PhD, CHT
University of Utah

Bob Wong, PhD
University of Utah—College of Nursing

Manuscript intended for submission to *Bone Marrow Transplant*

Abstract

Background

Preliminary research in exercise with patients undergoing hematopoietic stem cell transplantation shows similar benefits in physical performance and fatigue to research in cancer and physical activity. Small sample sizes, lack of randomization, and heterogeneity of settings limit the generalizability of studies into practice. In addition, there remains no consensus as to the type or dose of activity, or factors and approach that predict adoption and adherence of exercise in hematopoietic stem cell transplant patients.

Objective

Aim one (1) was to test the feasibility (recruitment rate, adherence, and attrition) of an exercise intervention versus attention control with patients undergoing a hematopoietic stem cell transplant. Aim two (2) examined the relationship between the exercise intervention versus the attention control on functional capacity, fatigue, perceived exertion, muscular strength, cardiovascular endurance, and pulmonary status.

Methods

Participants were stratified and randomly assigned to either the exercise intervention or the attention control group with 30 patients per arm. Groups met three times per week for approximately 1 hour. Participants were followed during stem cell collection (if applicable), chemotherapy, and recovery of their white count.

Results

The intervention group showed a significant time effects ($p = 0.041$) compared to the attention control group on functional performance as measured by the Functional

Performance Inventory. Significance was also found with the intervention group versus the control group with the Schwartz Cancer Fatigue Scale (p = >041). No effects were found with regards to muscular strength on the grip strength test. However, the step ascent test, which was also used to measure strength, showed significance between groups. Cardiovascular and pulmonary status as measured by the 6-Minute Walk was statistically significant for the intervention group (p = .001).

Conclusions

Hematopoietic stem cell transplant patients often come to treatment with some level of deconditioning; additionally, recovery from transplant can be complicated by diminished physical function, fatigue, and poor quality of life. This study provides additional support to proceed to a larger randomized clinical trial to replicate these findings and to determine type and intensity of exercise that will best benefit this unique population and to develop interventions that will facilitate exercise adherence.

Introduction and Background

Each year over 50,000 hematopoietic stem cell transplants (HSCT) are performed worldwide. Approximately, 25,000 allogeneic transplants are done annually along with over 30,000 autologous and cord blood transplants (Gratwohl, 2010). HSCT is considered a curative treatment for some hematological disorders such as Acute Myelogenous Leukemia, as well as some bone marrow failures (Russell et al., 1996; Russell, Brown, et al., 1997; Russell, Desai, et al., 1997; Russell et al., 1999). In other cases, transplant can impart good outcomes with a longer life expectancy.

Improvements in transplant technology and after care allow for increased survival rates. While there are thousands of survivors of stem cell transplant alive currently, we know that these patients face multiple challenges throughout their treatment and recovery course. Pretransplant status is often compromised in a substantial number of patients prior to transplant secondary to inactivity, side effects from medications, chemo-therapy, or the disease itself. Respiratory, skeletal muscle strength and maximal exercise capacity is reduced (White, Miller, & Ryan, 2005), making recovery of physical function even more demanding. Approximately 40-50% of patients continue to experience physical, psychological, and psychosocial stress up to 5 or more years after transplant (Bhatia et al., 2007). With mortality rates twice as high as that of the general population (Bhatia et al., 2007), these patients continue to live with many challenges that impact their health and quality of life.

The benefits of physical activity on functional performance, diminished symptoms, and improved quality of life in cancer patients are well established (Courneya, Friedenreich, Arthue, & Bobick, 1999; Galvao & Newton, 2005; Knols, Asronson, Uebelhart, Fransen, & Aufdemkampe, 2005; Stevinson, Lawlor, & Fox, 2004). The research in exercise with patients undergoing hematopoietic stem cell transplantation shows similar results such as improved physical function, decreased fatigue, and enhanced quality of life (Wiskemann & Huber, 2008). There is consistent evidence that exercise is safe and provides modest benefits with stem cell transplant patients.

While many of the studies document improvements to physical endurance, strength, and quality of life; few have provided interventions during actual treatment and the immediate post transplant recovery period (Dimeo et al., 1996; Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; Dimeo et al., 2003; Cunningham et al., 1986; Kim & Kim, 2006). These studies included either autologous transplant patients or allogeneic. Only one study to date has utilized an intervention during the treatment phase (Baumann, Kraut, Schule, Bloch, & Fauser, 2010) and included both allogeneic and autologous patients. Physical activity during this period of time is key to counteracting the effects of prolonged bed rest, such as muscle atrophy, cachexia, pneumonia, and loss of physical function.

This initial interventional trial evaluated the impact of a supervised exercise intervention versus an attention control group (both autologous and allogeneic transplant patients) during their treatment and immediate postrecovery period. Primary outcomes are fatigue, function, muscular strength, and cardio-pulmonary endurance. Tenets of the Theory of Planned Behavior have been included to guide in the understanding of exercise adherence behavior. This theory proposes that individuals will intend to perform a behavior when they evaluate it positively, believe that important others think they should perform it (subjective norms), and perceive it to be under their control. Variables of this theory include attitude toward exercise, perceived behavioral control, subjective norms, and intention.

Materials and Methods

Participants

A convenience sample of 60 participants was recruited from the approximately 340 adult transplant candidates annually that come for treatment at a major medical center in the upper Midwest. Inclusion criteria included: age 18 or older; able to speak, read, and write English; and medically cleared by their hematologist. This included acceptable pulmonary function test (DLCO < 50%), performance status (0-1 World Health Organization criteria), acceptable bone survey (no acute fractures), echocardiogram (ejection fraction >45%), negative infectious disease marker work-up, and acceptable renal function. Sixty participants consented and completed the study. The average age of participants was 53.6 (range 19-71) years and primarily Caucasian (N = 58; 96%). There were approximately equal numbers of females and males. Seventeen percent of the sample received an allogeneic transplant with the remainder an autologous transplant. Additional demographic information including diagnoses included can be seen in Table 9. Approval to conduct this study was granted by the Institutional Review Board of the appropriate institutions involved.

Measures

Dependent variables included feasibility, adherence, fatigue, function, perceived exertion, muscular strength, cardiovascular endurance, and determinants of exercise behavior.

Demographics were collected from the medical record and patients. Exercise activity was collected weekly via the Godin Leisure Time Questionnaire as well as a pre- and postassessment. This questionnaire includes the assessment of exercise behavior, both past and present. An independent evaluation of the Godin measure found it to be reliable and valid. It compared favorably to nine other self-report measures of exercise based on various criteria including test-retest (r = 0.62) and fitness indices (r = 0.56; Godin & Shepard, 1985). Feasibility is defined in aim one as the percentage of eligible participants who agreed to the study.

The variable of function was measured using the Functional Performance Inventory (Leidy, 1999). Functional performance, like exercise activity, was tested weekly as well as pre and post. This is a self-report measure in which performance is defined as day to day activities that people do to meet basic needs, fulfill usual roles, and maintain health and well-being. While there are many assessment tools to measure function, the Functional Performance Inventory was chosen because of its multidimensional conceptualization of function. Reliability and validity have been demonstrated (Cronbach alpha 0.93; Leidy, 1999).

Fatigue was measured using the Schwartz Cancer Fatigue Scale weekly and pre and post. This is a six-item checklist of adjectives with two components: physical fatigue and mental fatigue. This was chosen over other scales because it targeted cancer fatigue. Reliabilities for the total score and the sub scales are reported to be greater than 0.80 (Schwartz, 1998).

The Borg Scale of Perceived Exertion (Borg, 1998) was used to measure perceived exertion and aid in guiding participants during physical activity. It is based on the physical sensation a person experiences during exercise, including increased heart rate, respirations, perspiration, and muscle fatigue. Although this is a subjective measure, a person's exertion rating provides a fairly good estimate of the actual heart rate during exercise. A high correlation exists between a person's perceived heart and the actual heart rate during activity (Borg, 1998). A scale from 1 to 10 was used in this study.

A hydraulic hand dynamometer (Jamar® hydraulic hand dynamometer; Bissell Healthcare Corporation, Jackson, MI) was used to measure grip strength in participants' dominant hands. When used with a standardized measurement protocol, reliable measurements of muscle strength can be obtained (Bandinelli, Benvenuti, Del Lungo, Di Torio, & Ferrucci, 1999). An additional measure of physical function we used was the test of leg power or the step ascent test (a timed ascent/decent of one flight of stairs). This has demonstrated a strong correlation with functional status in frail men and women (Bean et al., 2002). Cardiovascular and pulmonary status was tested with the 6-minute walk. The American Thoracic Society has issued guidelines for administration of this test and reports validity and reliability for its use. Both groups were tested with these measures pre and post study.

Procedures

Participants were stratified by type of transplant and randomly assigned to the intervention or the control group. Both groups were asked to participate individually three times per week for approximately 30-60 minutes from the time they collected their stem cells, received their chemo-therapy, through the time of neutrophil engraftment which was defined as an absolute neutrophil count of 0.5 for 3 consecutive days or 1.0 for 1 day. This is an average of 30 days. Data collection took place from the first assessment and weekly through the final testing, approximately 30 days. Data were entered and stored in the RedCap data base which is password protected. All data were entered by the PI and double checked prior to entry. All self-report surveys were completed by patients and stored in folders which were coded with no identifying information. These were stored in a locked file cabinet and the PI was the only person with access.

Study sessions were scheduled after daily lab work and exams for the convenience for the participants. If hospitalized, they could participate if they were not febrile (>38.5C), thrombocytopenic (<20,000), or subjectively orthostatic, subjectively light headed or dizzy and /or blood pressure (<90/60 mmHg). Both groups were allowed to engage in physical activity outside the study. This was recorded on the weekly Godin Leisure Time Questionnaire.

Intervention Group

The intervention group consisted of the receipt of instructions on correct use of the equipment and proper positions for use of the Thera© Bands. They completed 10-12 repetitions of tricep and bicep curls, shoulder flexion, abduction, and extension. Aerobic activity included 20-30 minutes of exercise on either a treadmill or recumbent bicycle. The goal was to work at 60-75% of age predicted maximum heart rate which was guided by the Borg Scale of Perceived Exertion. This was based on guidelines from the American College of Sports Medicine (ACSM, 2006). The sessions were held in conjunction with daily out-patient visits as a convenience to patients. Participants were excluded from participation if they were febrile, thrombocytopenic and orthostatic.

Attention Control Group

The attention control group consisted of hourly sessions three times weekly. They participated in educational sessions. This included topics such as nutrition during transplant, guided imagery, relaxation training, sleep hygiene, and cognitive fitness. Similar to the intervention group, participants in the attention control could engage in physical activity outside the study.

Results

The Statistical Package for the Social Sciences (SPSS) version 19 was used to code and tabulate scores and provide summarized values when applicable. Descriptive statistics including frequency counts and percent statistics were computed for the demographic variables. Repeated measures ANOVA was used to test the interaction between and within groups.

Subjects

Of 72 eligible participants that were approached, 60 consented and completed this study. Reasons for nonparticipation included feeling overwhelmed by the treatment, lack of interest, and lack of time. Average age for the sample was 53.65 (range 19-71) years. There were approximately equal numbers of females and males in each group (47% female in the control group vs. 43% in the intervention group). Groups did not vary in terms of demographics.

For primary diagnosis, approximately 39% of participants in the control group were diagnosed with Multiple Myeloma, Amyloidosis, or Kappa Light chain, approximately 43% were diagnosed with Non-Hodgkin Lymphoma, and approximately 18% were diagnosed with Leukemia or MDS. Within the intervention group, approximately 39% of participants were diagnosed with Multiple Myeloma, Amyloidosis, or Kappa Light chain, approximately 28% were diagnosed with Non-Hodgkin Lymphoma, and approximately 33% were diagnosed with Leukemia or MDS. Results from the chi-square analysis indicate that frequency counts did not differ significantly between control and intervention groups, $\chi^2(2) = 2.463$, $p = .292$.

For type of transplant, approximately 8% of participants in the control group had an allogeneic transplant, whereas approximately 92% had an autologous transplant. Within the intervention group, approximately 23% of participants had an allogeneic transplant, while approximately 77% had an autologous transplant. Allogeneic transplant patients are known to have a significantly higher proportion of complications (Bhatia et al., 2007). Results from the chi-square analysis indicate that frequency counts were significantly different between control and intervention, $\chi^2(1) = 5.065$, $p = .024$. Randomization failed to equalize the groups and type of transplant and group type were not independent. There was a higher proportion of the more complication-prone allogeneic transplants in the intervention group than in the control group. Diagnoses, gender, ethnicity, and marital status are summarized in Table 9.

Adherence

All 60 of the participants included in this sample consented and completed the study. Adherence was defined as the number of prescribed sessions divided by the number completed. The average adherence rate for the control group was 69.27% and 79.63% for the intervention group. Participants were not allowed to exercise if they were thrombocytopenic, febrile, or orthostatic. Approximately 40% of participants were hospitalized during this study but continued to participate in the study unless they were medically unable (febrile, orthostatic, or thrombocytopenic). The intervention group was medically unable to participate approximately 20% of the time.

Functional Performance

In order to track functional performance over time, functional performance was measured at pre-, weeks 1, 2, 3, 4, and poststudy. This showed a significant difference by time (p = .041). The functional performance variable was skewed at the pre; however, with sample sized above 20 in each cell, ANOVA is robust to violations of this assumption (Tabachnick & Fidell, 2007). Overall, as the weeks passed, functional performance scores increased slightly then fell slightly, but not to the extent they were pre (see Figure 1). The pattern was stronger for the control group than for the intervention group, indicating that although functional performance scores increased for both groups over the time (indicating that ability got worse), the increase was higher for individuals in the control group (see Figure 1).

Results from the within subjects test revealed no significant differences existed between exercise time after controlling for control and experimental groups; *Wilks Lambda* (5, 55) = .847, p = .054, partial eta squared = .153. And finally, there was a significant difference in exercise scores between control and experimental groups; F(1, 58) = 11.764, p = .001, partial eta squared = .169.

Fatigue

Similarly, fatigue was also measured at pre, weeks 1, 2, 3, 4, and post. The groups showed a significant difference over time (p = .041). Across time, fatigue scores remained relatively stable for the intervention group; however; they increased for the control group (see Figure 2).

In addition to the profile test, a within subjects and between subjects test was conducted to determine if differences exist after controlling for groups, and time. Results from the within subjects test revealed a significant difference existed between fatigue time after controlling for control and experimental groups; *Wilks Lambda* (5, 54) = .423, $p < .000$, partial eta squared = .577. And finally, there was a significant difference in fatigue scores between control and experimental groups after controlling for time; $F(1, 58) = 7.756$, $p = .007$, partial eta squared = .118.

Strength

On the grip strength test, measures at pre and post were not significant ($p = .072$). An additional test of strength that was used was the step ascent test. The groups were not equal at baseline and this was controlled for in the analysis. The main effect of time was statistically significant ($F(1, 57) = 68.33$, $p = .001$), partial eta squared =.55 (see Table 10 and Figure 3). The interaction of time and group was also significant ($F(1, 57) = 16.60$, $p = .001$, partial eta squared = .226; see Table 10). The control group showed more of an increase, with scores from the intervention group remaining similar from baseline to posttest.

Cardiovascular Endurance

The main effect of time was statistically significant ($F(1,57) = 33.90$, $p = .001$) The mean walk scores for the intervention group were higher at baseline than for the control group. This was controlled for in the analysis. Overall, cardiopulmonary scores decreased from baseline to posttest. In addition, the interaction of time and group was statistically significant ($F(1,57) = 12.14$, $p =.001$, partial eta squared = .17). The control group showed more of a decline in their scores when compared to the intervention group (see Table 11 and Figure 4)

Discussion

Stem cell transplant patients typically come to treatment with various levels of deconditioning. Pre transplant status can be compromised secondary to inactivity, side-effects of medications and chemo-therapy and the disease itself. Respiratory, skeletal muscle strength and maximal exercise capacity is reduced (White et al., 2005). Despite the many advances in supportive care post transplant, this unique population often struggles with both physical and psychological rehabilitation needs well past the immediate recovery phase. This study extends the work of Courneya, Dimeo, and Baumann. Their work has shown physical exercise to be feasible and impart positive benefits during hospitalization (Dimeo et al., 1996; Dimeo et al., 1997). Bauman et al. (2010) validated and expanded this research by including both autologous and allogeneic participants as our study did. With regard to endurance and strength, our study, similar to the Baumann study, found that while endurance and strength scores decreased for both the intervention and control groups, the intervention group had less decline than did the control groups for both variables. This indicates that exercise during the active treatment phase aids in the maintenance of fitness. Our study further validates this previous research and demonstrates the feasibility of exercise during the treatment and immediate recovery period. Utilizing both autologous and allogeneic participants during active treatment, this feasibility study included both endurance and flexibility activities with a randomized intervention. Its results show that patients are willing to adhere to a supervised exercise program. Further, patients in this study maintained or improved fitness and experienced decreased fatigue.

Although limited sample size and the likely biased sample since people consenting to participation in the study were more likely to be motivated to exercise, this study reiterates that despite undergoing an intensive medical treatment, these patients can adhere to an exercise program. We observed improvements in function fatigue, strength, and with the intervention versus control groups, validating previous research with HSCT patients (Wiskemann & Huber, 2008). When looking at the average perceived exertion (Borg Scale; 1-10) scores for the six collection time points, both groups were able to exercise at a moderate level with an average of 3.63 for the control group and 3.23 for the intervention group. While this was not statistically significant, it does give us some guidance on the dose of activity that may help guide future research.

In summary, this work further validates preliminary evidence supporting the use of an exercise program with patients during the treatment and immediate post recovery phase from HSCT.

Table 9

Demographics

Control			Intervention		
Variable	*n*	Percent	Variable	*n*	Percent
Transplant Type			Transplant Type		
Allogeneic	5	8.3*	Allogeneic	14	23.3*
Autologous	55	91.7*	Autologous	46	76.7*
Primary Diagnosis			Primary Diagnosis		
Multiple Myeloma, Amyloidosis, or Kappa Light Chain Disease	11	39.3	Multiple Myeloma Amyloidosis, or Kappa Light Chain Disease	14	37.8
Non-Hodgkin Lymphoma	12	42.9	Non-Hodgkin Lymphoma	10	27.1
Leukemia or MDS	5	17.9	Leukemia or MDS	12	32.4
Hodgkin Lymphoma	0	0.0	Hodgkin Lymphoma	1	2.7
Gender			Gender		
Male	16	53.3	Male	17	56.7
Female	14	46.7	Female	13	43.3
Ethnicity			Ethnicity		
White	29	96.7	White	30	100.0
Hispanic	1	3.3	Hispanic	0	0.0
Marital Status			Marital Status		
Married	25	83.3	Married	24	80.0
Not Married	5	16.7	Not married	6	20.0

*Per chi-square, no differences in demographics except type of transplant, $X^2 = 5.065$, $p = .024$.

Table 10

Multivariate Model Summary for Strength—Step Ascent Test

Effect	Pillai's Trace	*F*	Hyp. *df*	Error *df*	*p*	Partial η^2
Time	.545	68.329	1	57	<.001	.545
Time * Group	.226	16.601	1	57	<.001	.226

Note. $N = 29$ for the control group and $N = 30$ for the intervention group. DV = Step Ascent test scores.

Table 11

Descriptive Statistics for Walk Scores, by Group

Group	Time Point	Min	Max	Mean	*SD*	Skew	*SD* of Skew
Control	Pre	800.00	2,030.00	1,467.41	348.54	-0.45	0.434
	Post	400.00	2,020.00	1,220.83	398.04	0.23	0.427
Intervention	Pre	1,220.00	2,560.00	1,735.03	282.68	0.99	0.427
	Post	1,100.00	2,615.00	1,674.67	306.39	0.79	0.427

Note. *N* = 29 for the control group and *N* = 30 for the intervention group.

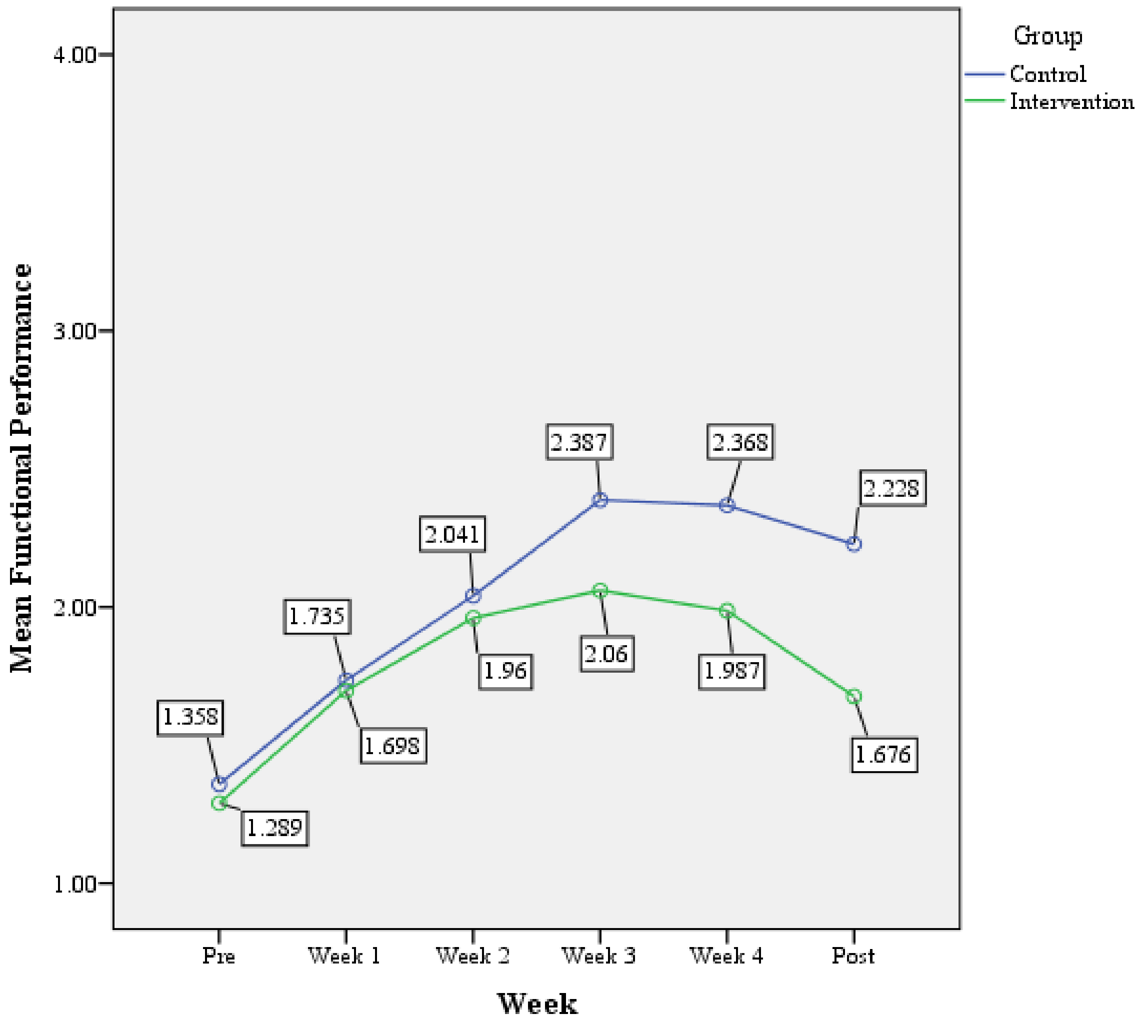


Figure 1. Plot of means for functional performance across time for intervention and control. Scale ranges from 1 = can do the activity easily with no difficulty to 4 = don't do for health reasons. If participant selected N/A, their average scores on the items they did respond to were calculated.

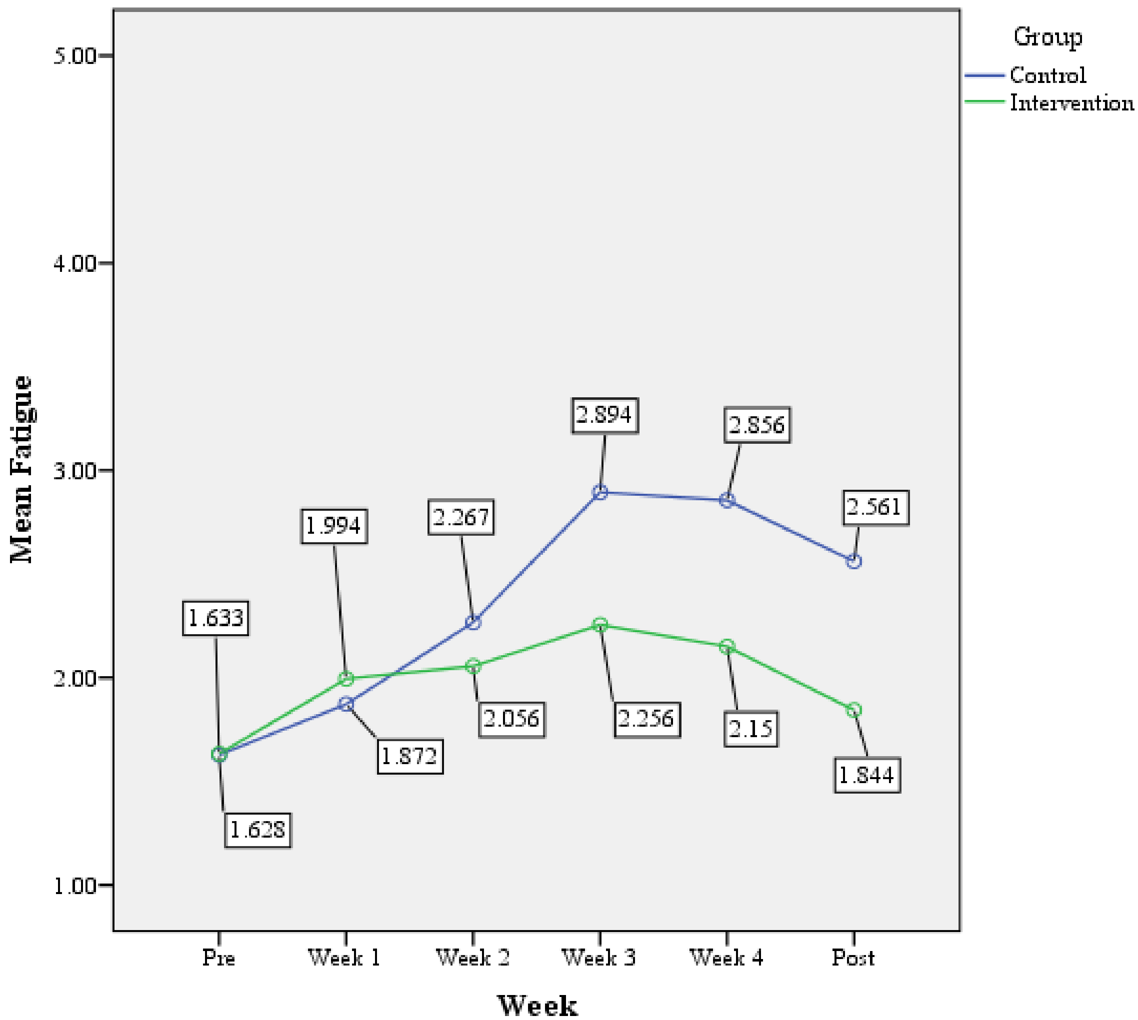


Figure 2. Plot of means for fatigue scores across time for control and intervention group. Scale ranges from 1 = not at all fatigued, 2 = a little, 3 = moderately, 4 = quite a bit, 5 = extremely.

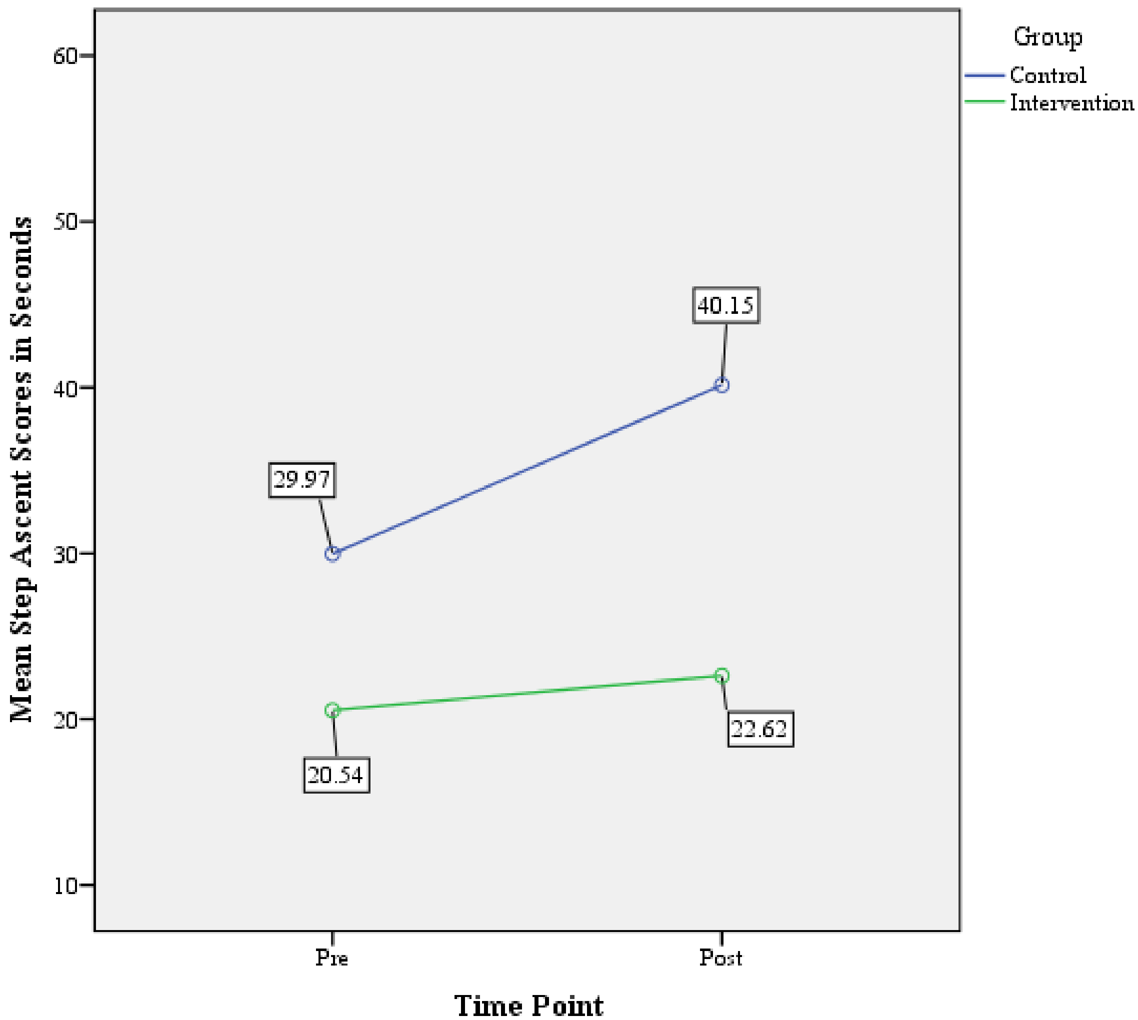


Figure 3. Plot of means for step-ascent scores at pre and post, by group.

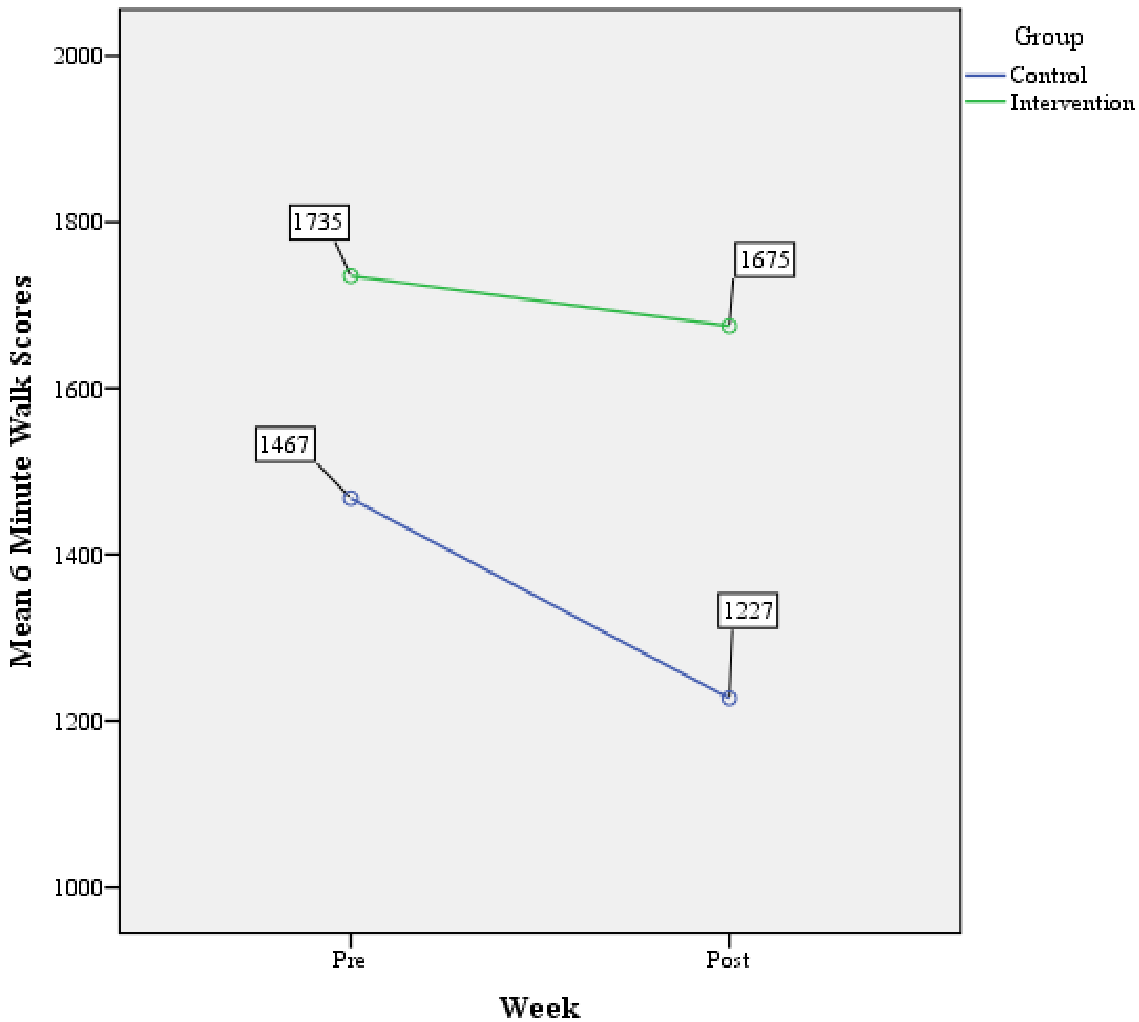


Figure 4. Plot of means for the 6-minute walk, by group.

References

Ajzen, I., Driver, B. L. (1992). Application of planned behavior to leisure choice. *Journal of Leisure and Rest, 24*(3), 207-224.

Ajzen, I., & Madden, T. J. (1986). Prediction of goal directed behavior: Attitudes, intentions, and perceived behavioral control. *Journal of Experimental Social Psychology, 22,* 453-474.

American College of Sports Medicine. (2006). *ACSM's guidelines for exercise testing and prescription* (7th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Bandinelli, S., Benvenuti, E., Del Lungo, I., Di Torio, A., & Ferrucci, L. (1999). Measuring muscle strength of the lower limbs by hand-held dynamometer: A standard protocol. *Aging, 11*(5), 287-293.

Baumann, F. T., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation, 35,* 355-362.

Bean, J. F., Kiely, D. K., Herman, S., Leveille, S. G., Mizer, K., Frontera, W., & Fielding, R. A. (2002). The relationship between leg power and physical performance in mobility-limited older people. *Journal of the American Geriatric Society*. 50, 461-467.

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker S., Gurney, J. G., . . . Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: Report from the Bone Marrow Transplant Survivor Study. *Blood, 110*(10), 3787-3792.

Borg, G. (1998). *Borg's perceived exertion and pain*. Champaign, IL: Human Kinetics.

Courneya, K., Friedenreich, C. M., Arthue, K., & Bobick, T. M. (1999). Understanding exercise motivation in colorectal patients: A prospective study using the theory of planned behavior. *Rehabilitation Psychology, 44*(1), 68-84.

Cunningham, K., Keats, M. R., & Turner, A. R. (2000). Social cognitive determinants of hospital-based exercise in cancer patients following high dose chemotherapy and bone marrow transplantation. *International Journal of Behavioral Medicine, 7*(3), 189-203.

Dimeo, F., Bertz, H., Finke, Fetscher, S., Mertelsmann, R., & Keul, J. (1996). An aerobic exercise program for patients with haematological malignancies after bone marrow transplantation. *Bone Marrow Transplant, 18,* 157-160.

Dimeo, F., Fetscher, S., Lange, W., Mertelsmann, R., & Keul, J. (1997). Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood*, *90*, 3390-3394.

Dimeo, F., Schwartz, S., Fietz, T., Wanjura, T., Boning, D., & Thiel, E. (2003). Effects of endurance training on the physical performance of patients with hematological malignancies during chemotherapy. *Supportive Care Cancer*, *11*, 623-628.

Galvao, D. A., & Newton, R. U. (2005). Review of exercise intervention studies in cancer patients. *Journal of Clinical Oncology*, *23*(4), 899-909.

Godin, G., & Shepard, R. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Sciences*, *10*(3), 141-146.

Gratwohl, A., Baldomero, H., Aljurf, M., Pasquini, M. C., Bouzas, L. F., Yoshimi, A., . . . Kodera, Y. (2010). Hematopoietic stem cell transplantation: A global perspective. *Journal of the American Medical Association, 303*(16, 1617-1624.

Jones, L., Courneya, K. S., Vallanec, J. K., Ladha, A. B., Mant, M. J., Belch, A. R., & Reiman, T. (2006). Understanding the determinants of exercise intentions in multiple myeloma. *Cancer Nursing*, *29*(3), 167-175.

Kim, S., & Kim, H. S. (2006). A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. E*uropean Journal of Cancer Care—English Version*, *15*, 453-457.

Knols, R., Asronson, N. K., Uebelhart, D., Fransen, J., & Aufdemkampe, G. (2005). Physical exercise in cancer patients during and after medical treatment: A systematic review of randomized and controlled clinical trials. *Journal of Clinical Oncology*, *23*(16), 3830-3842.

Leidy, N. K. (1999). Psychometric properties of the functional performance inventory in patients with chronic obstructive pulmonary disease. *Nursing Research*, *48*(1), 20-28.

Rhodes, R., & Courneya, K. S. (2003) Investigating multiple components of attitude, subjective norm and perceived control: An examination of the theory of planned behavior in the exercise domain. *British Journal of Social Psychology*, *42*(pt. 1), 19-36.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1996). Allogeneic blood cell transplants for haematological malignancy: Preliminary comparison of outcomes with bone marrow transplantation. *Bone Marrow Transplant, 17*, 703-708.

Russell, J. A., Brown, C., Bowen, T., Luider, J., Ruether, J. D., Stewart, D., . . . Klassen, J. (1997). Second allogeneic transplants for leukemia using blood instead of bone marrow as a source of hematopoietic cells. *Bone Marrow Transplant, 18,* 501-505.

Russell, J. A., Desai, S., Herbut, B., Brown, C., Luider, J., Ruether, J. D., . . . Klassen, J. (1997). Partially mismatched blood cell transplants for high-risk hematologic malignancy. *Bone Marrow Transplant, 19,* 861-866.

Russell, J. A., Larratt, L., Brown, C., Turner, A. R., Chaudhry, A., Booth, K., . . . Poon, M. C. (1999). Allogeneic blood stem cell and bone marrow transplantation for acute myelogenous leukemia and myelodysplasia: Influence of stem cell source on outcome. *Bone Marrow Transplant, 24,* 1177-1183.

Schwartz, A. I. (1998). The Schwartz Cancer Fatigue Scale: Testing, reliability and validity. *Oncology Nursing Forum, 25*(4), 717-722.

Stevinson, C., Lawlor, D. A., & Fox, K. R. (2004). Exercise interventions for cancer patients: A systematic review of controlled trials. *Cancer Causes Control, 15*(10), 1035-1056.

Tabachnick, B. G., & Fidell, L., S. (2007). *Using multivariate statistics* (5th ed.). Boston, MA: Allyn & Bacon.

White, A., Miller, K. B., & Ryan, H. F. (2005). Impaired respiratory and skeletal muscle strength in patients prior to hematpoietic stem cell transplantation. *Chest, 128*, 145-152.

Wiskemann, J., & Huber, G. (2008). Physical exercise as adjuvant therapy for patients undergoing hemtopoietic stem cell transplantation. *Bone Marrow Transplant, 41*, 321-32

CHAPTER 4

THE THEORY OF PLANNED BEHAVIOR: A FRAMEWORK TO UNDERSTAND THE DETERMINANTS OF EXERCISE INTENTIONS IN STEM CELL TRANSPLANT PATIENTS

Randi Hoffmann, RN, PhD (c)
Mayo Clinic, Rochester, Minnesota

Kathi Mooney, RN, PhD, FAAN
University of Utah—College of Nursing

Debra Barton, RN, PhD, AOCN, FAAN
Mayo Clinic, Rochester, Minnesota

Erin Rothwell, PhD, TRS, CTRS, CRSS
University of Utah—College of Nursing

Paul C. LaStayo, PT, PhD, CHT
University of Utah

Bob Wong, PhD
University of Utah—College of Nursing

Manuscript intended for submission to *Bone Marrow Transplant*

Abstract

Purpose

Preliminary research in exercise with patients undergoing hematopoietic stem cell transplantation shows similar benefits in physical performance and fatigue to research in cancer and physical activity. Adherence has been a challenge in much of the related research. Here, we report on the predictors of adherence in exercise interventions with stem cell transplant patients with a focus on the application of the Theory of Planned Behavior.

Methods

Hematopoietic stem cell transplant patients (N = 60) were randomly assigned to an individually supervised exercise intervention or attention control group during active treatment. Variables included function, fatigue, strength, cardio-pulmonary function, and the motivational variables from the Theory of Planned Behavior. Adherence was assessed by objective attendance records.

Results

Adherence to supervised exercise was 79.63%. Results for function, fatigue, strength and cardio-pulmonary status were maintained or improved (results are reported elsewhere). Variables of the Theory of Planned Behavior were examined with multiple regression to determine their contribution to exercise behavior. The overall model was found to contribute 20.3 % to the variance in exercise behavior. While no individual variable was found to predict exercise on its own, perceived behavioral control (p = .09) and intention (p = .19) trended towards significance.

Conclusion

Adherence to supervised exercise in this study was partially explained by the Theory of Planned Behavior model. This model may help to inform the development of interventions that improve adherence to exercise during stem cell transplant and the post recovery period.

Introduction

Exercise therapy in cancer and hematopoietic stem cell transplant(HCST) survivors has gained interest. Over the past several decades physical activity has been shown to play an important role in prevention of certain cancers such as breast cancer, colon and prostate cancer (World Cancer Research Fund & American Institute for Cancer Research, 2007; Friedenreich, Courneya, & Bryant, 2002). It has become widely accepted that exercise is a viable therapy to attenuate the many side effects of chemotherapy including both psychological and physical symptoms in cancer patients such as fatigue, diminished cardiac and pulmonary function, limited muscular strength, and cachexia (Andrykowski & Altmaier, 1995; Andrykowski et al., 2005). There is a growing body of research that demonstrates similar outcomes for survivors of hematopoietic stem cell transplant. In this population, exercise has shown promising results with improvements shown in fatigue, muscle strength, endurance, and quality of life.

Advances in transplant technology and after care allow for increased survival. While there are thousands of survivors of stem cell transplant alive currently, we know that these patients face multiple challenges throughout their treatment and recovery course. Pretransplant status is often compromised in a substantial number of patients prior to transplant because of inactivity, side effects from medications, chemo-therapy, or the disease itself. In the pretransplant phase, respiratory, skeletal muscle strength, and maximal exercise capacity is reduced (White, Miller, & Ryan, 2005), making recovery of physical function posttransplant even more demanding. Approximately 40-50% of patients continue to experience physical, psychological, and psychosocial stress up to 5 or more years after transplant (Bhatia et al., 2007). With mortality rates twice as high as that of the general population (Bhatia et al., 2007), these patients continue to live with many challenges that impact their health and quality of life. Exercise shows promise in mitigating some of these challenging long-term effects of treatment.

A number of the research studies have examined exercise in the HSCT population at various trajectories from active treatment through recovery (Baumann, Kraut, Schule, Block, & Fauser, 2010; Cunningham et al., 1986; Dimeo, Fetscher, Lnaage, Mertelsmann, & Keul, 1997; Dimeo, Finke, Fetscher, Mertelsmann, & Keul, 1996; Dimeo et al., 2003; Kim & Kim, 2006). Some exercise studies have been in the out-patient setting (Dimeo et al., 1997; Dimeo et al., 1996; Hayes, Davies, Parker, Bashford, & Green, 2004; Hayes, Davies, Parker, Bashford, & Newman, 2004) while others have been home-based (Carlson, Smith, Russell, Fibich, & Whittaker, 2006; Coleman et al., 2003; Decker, Turner-McGlade, & Fehir, 1989). Still others were initiated during hospitalization and continued afterward (Dimeo et al., 1996; Mello, Tanaka, & Dulley, 2003; Wilson, Jacobsen, & Fields, 2005). Average adherence to exercise for these studies was 85%. The rate for the home based (without supervision) was lower at 68% while in the supervised exercise studies, both in and outpatient settings, were above 90%.

While the adherence rates for the previously discussed studies are positive, overall adherence to long-term exercise is quite poor. According to a study released by the Centers for Disease Control and Prevention (2007), only 50% of healthy Americans are meeting the recommended guidelines for regular exercise. Those recovering from major medical conditions face additional challenges. One year after a major cardiac event, only 37% of patients sampled were adhering to a three times per week recommended regimen (Dolansky, Stepanczuk, Charvat, & Moore, 2010). One study of exercise in Non-Hodgkin Lymphoma survivors, including some who received stem cell transplants, found that the majority of participants were not meeting the Canadian guidelines for physical activity of at least 150 minutes of moderate to vigorous activity per week (Vallance, Courneya, Jones, & Reiman, 2006). Twenty-five percent of the 431 patients studied had received a stem cell transplant. These findings are consistent with survey studies in breast cancer (Courneya & Friedenreich, 1997) colorectal (Courneya & Friedenreich, 1997), and multiple myeloma (Jones, et al., 2006).

Maximizing adherence and maintenance of physical activity is critical to the development of research designs and translation into clinical practice. Defining the elements that influence adherence to physical activity would be a significant contribution to the development and maintenance of interventions aimed at these cancer survivors. A number of theories have been examined including social-cognitive theory (Basen-Engquist et al., 2011; Rogers et al., 2011), the self-determination theory (Milne, Wallman, Guifoyle, Gordon, & Courneya, 2008; Wilson et al., 2005) and the attribution theory (Courneya, Friedenreich, Sela, Quinney, & Rhodes, 2002).

Courneya and his colleagues have utilized the Theory of Planned Behavior (TPB) in multiple studies and in a variety of cancer populations including breast, prostate, colorectal, non-Hodgkin's lymphoma, multiple myeloma, and one study with bone marrow transplant patients (Blanchard, Courneya, Rodgers, & Murnaghan, 2002; Coleman et al., 2003; Courneya, 1997; Courneya, Friedenreich, Arthue, & Bobick, 1999; Courneya, Keats, & Turner, 2000; Courneya, Vallance, Jones, & Reiman, 2005). To date, there are no current studies examining the use of the correlates of the theory of planned behavior with hematopoietic stem cells transplant patients. One of the objectives of this study was to examine the relationships of the tenets of TPB and how they contributed to variance in exercise behavior. The hypothesis was that the variables of TPB would have a medium correlation (i.e., r = 0.3-0.5) with supervised and patient reported physical activity.

Theoretical Framework

This study was guided by the theory of planned behavior (Ajzen, 2002). This theory suggests that an immediate predictor of physical activity is a person's intention which has three components. Attitude is a positive or negative interpretation of the performance. Subjective norms are the perceived social pressure one might experience to either perform or not perform the behavior. Perceived behavioral control is the perceived ease or difficulty of engaging in the behavior (Figure 5). This can have a direct and indirect impact on the performance of that behavior. This can also be thought of as the ease or difficulty in performance of the action. Azjen and Driver (1992) noted that perceived behavioral control should capture an individual's confidence to perform the behavior (i.e., self-efficacy) as well as the individual's belief that they have control over the behavior.

Attitude can be divided into affective attitude which refers to the feelings elicited by the possibility of performing the behavior; instrumental attitude that refers to the rational evaluation of potential advantages of performing the behavior. According to Azjen and Driver (1992), attitudes are grounded in behavioral beliefs which include the perceived advantages and disadvantages of performing the behavior. Perceived behavioral control is the perceived confidence and control over being able to perform the activity. This encompasses perceived controllability which refers to the individual's control over performing the behaviors and the perceived self-efficacy, which refers to the ease or difficulty of performing the behavior. Again, according to Azjen and Driver (1992), perceived behavioral control is grounded in control beliefs, which include the extent to which certain helpful or preventative factors could affect behavior. In combination with favorable intention, perceived behavioral control can directly impact behavior. Subjective norms refers to perceived social pressure to perform or not perform the behavior in question. The more positive the attitude and subjective norm and the higher the perceived behavioral control, the greater a person's intention to engage in the behavior in question (Courneya, Karvinen, & Vallance, 2007).

Methods

A convenience sample of 60 participants beginning allogeneic or autologous stem cell transplant were recruited from the approximately 340 adult stem cell transplant candidates that annually that come for stem cell transplantation at the Mayo Clinic, Rochester, Minnesota. Eligibility criteria included: age 18 or older; able to speak, read and write English; and medically cleared by their hematologist. This included acceptable pulmonary function tests (DLCO < 50 %); performance status (0-1 World Health Organization criteria); acceptable bone survey (no acute lesions); echocardiogram (ejection fraction > 45%); infectious disease markers work-up; and acceptable renal function. Approval to conduct this study was granted by the Institutional Review Board of all institutions involved.

Design and Procedure

This study was a randomized clinical trial. Participants were randomly assigned to the exercise intervention group or the attention control group. The intervention group participated in supervised exercise sessions while the attention control group participated in educational sessions that provided information on how to more effectively deal with side effects of treatment. Topics related to exercise and fatigue were not included. Both groups met three times weekly and could exercise outside the study. For the purposes of the study, physical activity was recorded weekly on the Godin Leisure Time Questionnaire (Godin & Shepard, 1985). This is a self-report measure which captures physical activity completed in 15-minute increments and defines them as strenuous, moderate, or mild. Participants count the number of 15-minute increments that they have completed in each category.

The Theory of Planned Behavior variable assessment was based on Ajzen's established guidelines (Azjen, 2006). The standardized items have been shown to be valid and reliable from previous research in the cancer population (Jones et al., 2007; McNeely et al., 2012; Peddle et al., 2009). Items were altered to reflect the context of the stem cell transplant population. Each item was scored on a 7-point adjective scale with 1 being a negative response and 7 being a positive response.

Attitude

Six items were used to assess affective (e.g., enjoyable/unenjoyable, pleasurable/painful, fun/boring) and instrumental (e.g., useful/useless, beneficial/harmful, important/unimportant) attitudes. The scales were preceded by the statement "I think that for me to perform regular physical activity over the next month would be . . . ." Seven-point scales were used with the descriptors of extremely (1 and 7), quite (2 and 6), and slightly (3 and 5; 4 was neutral). Affective and instrumental attitudes were combined in to the variable of attitude. Internal consistency as measured by Cronbach α was .824.

Subjective Norms

Three items were used to assess injunctive norms (approving/disapproving, encouraging/discouraging, supportive/unsupportive). The scales were preceded by the statement "I think that if I engaged in regular physical activity over the next month, most people who are important to me . . . ." Internal consistency for subjective norms as measured by Cronbach α was .938.

Perceived Behavioral Control

Three items were used to assess variables related to perceived behavioral control: (a) "If really motivated" followed by extremely easy to extremely hard to exercise over the next month; (b) "How confident would you be that you could exercise over the next month?" followed by not at all confident to extremely confident; and (c) "How much control do you feel that you have in exercising over the next month?" followed by very little control to complete control. Internal consistency for these variables as measured by Cronbach α was .861.

Intention

Three items were used to assess intention: (a) I intend to exercise regularly over the next month (strongly disagree to strongly agree), (f) I intend to exercise at least three times a week (strongly disagree to strongly agree), and (c) I intend to exercise with a blank to fill in with a number of times the participant thought that they intended to exercise over the next month. Internal consistency for intention as measured by Cronbach α was .713.

Adherence

Adherence was the number of actual sessions the intervention group engaged in subtracted from the prescribed number. For safety reasons, the experimental group was not allowed to exercise if febrile (>38.5 C), thrombocytopenic (platelets 20,000 or lower), orthostatic on previous exam (systolic less than 70 and a diastolic less than 40) or subjectively light headed or dizzy, have chest pain or oxygenation levels at rest that are less than 90% (via pulse Oximetry) and/or pain greater 5 of 10 with medication and a heart rate below 50. These restrictions were not as critical for those in the control group who only needed to attend an individualized educational series.

The principal investigator collected all the demographic and medical information via self-report and the medical record review. This included age, gender, diagnoses, transplant type, marital status, income, education, employment status, and ethnicity.

Statistical Analysis—Results

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 19. Descriptive statistics including frequency counts, and percent statistics were computed for the demographic variables. Repeated measures ANOVA was used to test the interaction between and within the groups and multiple regression was used to evaluate the components of the Theory of Planned Behavior.

Of 72 eligible participants that were approached, 60 consented and completed this study. Reasons for nonparticipation included feeling overwhelmed by the treatment, lack of interest, and lack of time. Average age for the sample was 53.65 (range 19-71) years. There were approximately equal numbers of females and males in each group (47% female in the control group vs. 43% in the intervention group). Groups did not vary in terms of demographics. Ten percent received allogeneic transplants while the remainder received their own cells (autologous). Multiple Myeloma and Non-Hodgkin Lymphoma accounted for approximately 70% of the medical diagnoses with the remainder including Acute Myelogenous Leukemia, Chronic Lymphocytic Leukemia, Hodgkin's Lymphoma, Myelodysplastic Syndrome and Amyloidosis. The typical participant was Caucasian, married and had 2 or more years of college education.

The average adherence rate for the control group was 69.27% and 79.63% for the intervention group. As detailed previously, intervention participants were not allowed to exercise if they were thrombocytopenic, febrile, or orthostatic. Sixty percent of participants were hospitalized during their participation for an average hospital stay of 4 days. Forty percent remained as out-patients and participated coming from near-by lodging. Both groups were engaged in the study for approximately 6 weeks.

Attitude, perceived behavioral control, subjective norms, and intention to exercise were measured by multiple regression. The variables of intention to exercise, attitude towards exercise, perceived behavioral control, and subjective norms were analyzed to determine if they were independent predictors of exercise behavior as measured by the Godin Leisure Time Questionnaire. The Godin Leisure Time Questionnaire captures self-reported time exercised per week. While no individual variable was found to predict exercise on its own, the group of variables as a whole predicted 20.3% of the variance in exercise behavior. Perceived behavioral control (p = .09) and intention (p = .19) were the most important determinants but were not statistically significant individually. Attitude toward exercise (p = .92) and subjective norms (p = .33) were not as important in determining exercise behavior.

Discussion

The present study provides additional support that the Theory of Planned Behavior is a useful theoretical framework for understanding the determinants of physical exercise during stem cell transplantation and recovery. The overall model showed that 20.3% of the variance in exercise behavior could be explained by the model. This finding is generally consistent with the findings of a meta-analysis where the Theory of Planned Behavior accounted for 27.4% of the variance in exercise adherence and 44.5% of the variance in intention in the general population (Hager, Chatzisarantis, & Biddle, 2002). In studies of the Theory of Planned Behavior with cancer survivors, the model has been found to explain between 14 and 35% of the variance in exercise behavior and 23-49% of the variance in exercise intention (Blanchard et al., 2002; Courneya, Blanchard, & Laing, 2001; Courneya & Friedenreich, 1997, 1999).

Despite the existing literature testing showing that intention was one of the most important predictors of behavior in both the general and cancer populations, perceived behavioral control in this study emerged as a more important predictor of exercise with the stem cell population. These findings suggest that participants may have become more confident in their ability to exercise with an accessible supervised program in place that allowed them to engage in activity at their own pace.

Self-efficacy and confidence are key components of perceived behavioral control and previous studies in cancer patients have shown that perceived behavioral control is an independent correlate of exercise behavior and adherence (Karvinen et al., 2007; Peddle et al., 2009). In our study, we found that perceived behavioral control was a key construct in explaining exercise behavior. These findings extend that to a unique subset of cancer patients, stem cell transplant survivors. The results suggest that the development of strategies to improve participants' confidence and feeling of control, may improve their intention to exercise and adherence.

Attitude and subjective norms in our study did not emerge as significant when compared with perceived behavioral control and intention. This is similar to previous studies with bone marrow transplant patients (Courneya et al., 2000), two colorectal studies (Courneya et al., 1997, 1999) and one prostate survivor study (Blanchard et al., 2002). These studies included primarily male survivors. Other studies have shown subjective norms to be significant determinants of exercise intention as in the case of three breast cancer studies (Courneya et al., 2001; Courneya & Fredenreich, 1997, 1999). This highlights the possibility that there may be gender differences that account for this variation. While the theory of planned behavior has shown utility as a framework to understand cognitive determinants of exercise behavior, these differences also highlight the inconsistent pattern of theory of planned behavior association across various cancer populations. Given the various findings, this may also reflect the differences in medical context and demographics of cancer populations studied. At a minimum, larger prospective studies are warranted to further investigate and confirm these findings.

A number of limitations should be considered when interpreting the results and planning for future research. While this study was prospective in design, it only followed stem cell transplant patients from their treatment through stem cell recovery. Adherence after transplant should be studied and would more accurately reflect how the theory of planned behavior impacts long-term adherence. The sample size was also limited and could be biased since participants who volunteered for this study were more likely to be interested in interested in physical exercise. However, we had a low decline rate (18%). While the actual intervention involved supervised exercise, any activity outside the study was self-reported and may not accurately reflect actual exercise. Further, we did not collect other factors outside of the model such as perceived barriers to physical exercise that might contribute to exercise adherence. Since the model only explained 20.3% of the variance, other factors, not measured in this model, could contribute to a fuller understanding of exercise adherence.

Despite these limitations, these findings indicate that intention and perceived behavioral control were the strongest correlates of physical activity in a sample of stem cell transplant patients which included both allogeneic and autologous transplant types. The current study provides some evidence of the utility of the Theory of Planned Behavior as a tool to elucidate cognitive-behavioral influences on exercise behavior in stem cell transplant patients. These results extend previous study by Courneya and his colleagues with stem cell transplant patients and multiple other cancer populations with the inclusion of both transplant types during active treatment. Understanding factors that influence stem cell transplant patients' willingness to adhere to an exercise program during and after treatment is essential to assuring that patients incorporate exercise in their program of recovery and receive the related benefits. Behavioral theories can contribute to understanding these important cognitive-behavioral factors.

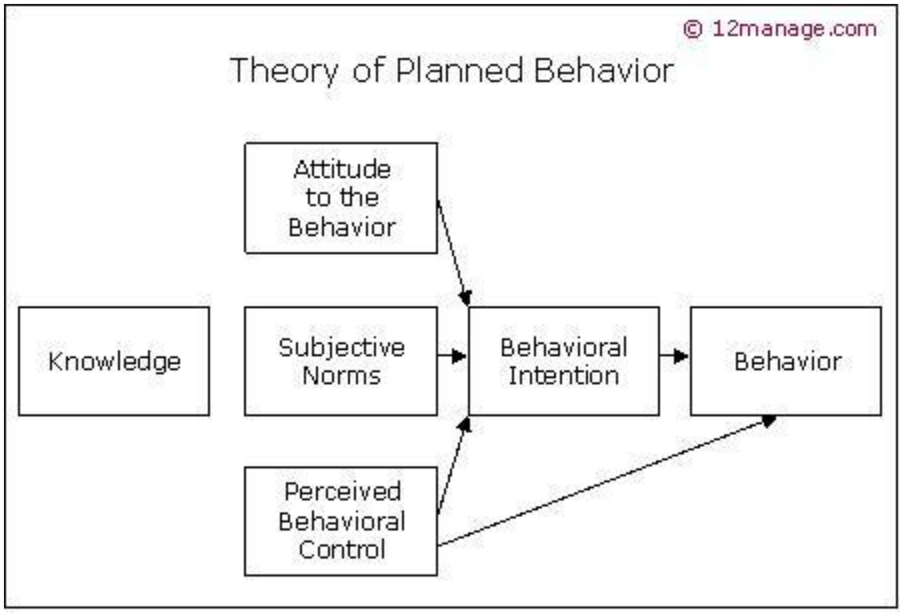


Figure 5. The theory of planned behavior. Reprinted with permission from I. Ajzen and B. L. Driver, 1992, "Application of Planned Behavior to Leisure Choice," *Journal of Leisure and Rest, 24*(3), 207-224.

References

Ajzen, I. (2006). Constructing a TPB questionnaire: Conceptual and methodological considerations. Retrieved from http://people.umass.edu/azjen/pdf /tpb.measurements.pdf

Ajzen, I., & Driver, B. L. (1992). Application of planned behavior to leisure choice. *Journal of Leisure and Rest, 24*(3), 207-224.

Andrykowski, M. B., & Altmaier, E. M. (1995). Quality of life following bone marrow transplantation: Findings from a multicentric study. *British Journal of Cancer, 71,* 1322-1329.

Andrykowski, M. B., Bishop, M., Hahn, E. A., Cella, D. F., Beaumont, J. L., Brady, M. J., . . . Wingard, J. R. (2005). Long-term health related quality of life, growth and spiritual well-being after hematopoietic stem-cell transplantation. *Journal of Clinical Oncology, 23*(3), 599-608.

Basen-Engquist, K., Carmack, C. L., Perkins, H., Hughes, D., Serice, S., Scruggs, S., . . . Waters, A. (2011). Design of the steps to health study of physical activity in survivors of endometrial cancer: A cognitive theory model. *Psychology of Sport and Exercise, 12*(1), 27-35.

Baumann, F., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation, 45,* 355-362.

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker, S., Gurney, J. G., . . . Nadermanee, A. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: Report from the Bone Marrow Transplant Survivor Study. *Blood, 110*(10), 3874-3789.

Blanchard, C., Courneya, K. S., Rodgers, W. M., & Murnaghan, D. M. (2002). Determinants of exercise intention and behavior in survivors of breast and prostate cancer: An application of the Theory of Planned Behavior. *Cancer Nursing, 25*(2), 88-95.

Carlson, L. E., Smith, D., Russell, J., Fibich, C., & Whittaker, T. (2006). Individualized exercise program for the treatment of severe fatigue in patients after allogeneic hematopoietic stem-cell transplant: A pilot study. *Bone Marrow Transplantation, 37,* 945–954.

Centers for Disease Control and Prevention. (2007). *Health behaviors of adults: United States, 2005-2007*. Hyattsville, MD: Author.

Cohen, J. (1988). *Statistical analysis for the behavioral sciences*. Philadelphia, PA: Lawrence Erlbaum Associates.

Coleman, E., Coon, S., Hall-Barrow, J., Richards, K., Gaylor, D., & Stewart, B. (2003). Feasibility of exercise during treatment for multiple myeloma. *Cancer Nursing, 26*, 410-419.

Courneya, K., Blanchard, C. M., & Laing, D. (2001). Exercise adherence in breast cancer survivors training for a Dragon boat race competition: A preliminary investigation. *Psycho-oncology*, *10*, 444-452.

Courneya, K., & Friedenreich, C. M. (1997). Determinants of exercise during colorectal cancer treatment: An application of the theory of planned behavior. *Oncology Nursing Forum, 24*(10), 1715-1723.

Courneya, K., & Friedenreich, C. M. (1999). Utility of the theory of planned behavior for understanding exercise during breast cancer treatment. *Psycho-oncology, 8*, 112-122.

Courneya, K., Friedenreich, C. M., Arthue, K., & Bobick, T. M. (1999). Understanding exercise motivation in colorectal patients: A prospective study using the theory of planned behavior. *Rehabilitation Psychology, 44*(1), 68-84.

Courneya, K., Friedenreich, C. M., Sela, R. A., Quinney, H. A., & Rhodes, R. E. (2002). Correlates of adherence and contamination in a randomized controlled trial of exercise in cancer survivors: An application of the theory of planned behavior and the five factor model of personality. *Annals of Behavioral Medicine*, *24*, 257-268.

Courneya, K., Karvinen, K. H., & Vallance, J. K. H. (2007). Exercise motivation and behavior change. In M. Feuerstein (Ed.), *Handbook of cancer survivorship* (pp. 113-132). New York, NY: Springer.

Courneya, K., Keats, M. R., & Turner, A. R. (2000). Social cognitive determinants of hospital-based exercise in cancer patients following high dose chemotherapy and bone marrow transplantation. *International Journal of Behavioral Medicine*, *7*(3), 189-203.

Courneya, K., Vallance, J. K. H., Jones, L. W., & Reiman, T. (2005) Correlates of exercise intentions in non-Hodgkin's lymphoma survivors: An application of the theory of planned behavior. *Journal of Sports Medicine Psychology*, *27*, 335-347.

Cunningham, B., Morris, G., Cheney, C. L., Buergel, N., Aker, S. N., & Lenssen, P. (1986). Effects of resistive exercise on skeletal muscle in marrow transplant recipients receiving total parental nutrition. *Journal of Parenteral Enteral Nutrition, 10*, 558-563.

Decker, W., Turner-McGlade, J., & Fehir, K. M. (1989). Psychological aspects and the physiological effects of a cardiopulmonary exercise program in patients undergoing bone marrow transplantation (BMT) for Acute Leukemia (AL). *Transplant Proceedings, 21*(1, Pt. 3), 3068-3069.

Dimeo, F., Fetscher, S., Lnaage, W., Mertelsmann, R., & Keul, J. (1997). Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood, 90*, 3390-3394.

Dimeo, F., Finke, J., Fetscher, S., Mertelsmann, R., & Keul, J. (1996). An aerobic exercise program for patients with haemotological malignancies after bone marrow transplantation. *Bone Marrow Transplant, 18,* 1157-1160.

Dimeo, F., Schwartz, S., Fietz, T., Wanjura, T., Boning, D., & Thiel, E. (2003). Effects of endurance training on the physical performance of patients with hematological malignancies during chemotherapy. *Supportive Care Cancer, 1,* 623-628.

Dolansky, M. A., Stepanczuk, B., Charvat, J. M., & Moore, S. M. (2010). Women's and men's exercise adherence after a cardiac event: Does age make a difference? *Research in Gerontological Nursing, 3*(1), 30-38.

Friedenreich, C. M., Courneya, K. S., & Bryant, H. E. (2002). Case-control study of anthropometric measures and breast cancer risk. *International Journal of Cancer, 99,* 445-452.

Godin, G., & Shepard, A. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Science, 10,* 141-146.

Hager, M. S., Chatzisarantis, N. L. D., & Biddle, S. J. H. (2002). A meta-analysis review of the theories of reasoned action and planned behavior in physical activity: Predictive validity and the contribution of additional variables. *Journal of Sport and Exercise Physiology, 24,* 3-32.

Hayes, S., Davies, P. S., Parker, T., Bashford, J., & Green, A. (2004). Role of a mixed-type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *British Journal of Sports Medicine, 38,* 304-309.

Hayes, S., Davies, P. S., Parker, T., Bashford, J., & Newman, B. (2004). Quality of life changes following peripheral blood stem cell transplantation and participation in a mixed-type, moderate-intensity, exercise program. *Bone Marrow Transplantation, 33,* 553–558.

Jones, L., Courneya, K. S., Vallance, J. K., Ladha, A. B., Mant, M. J., Belch, A. R., & Reiman, T. (2006). Understanding the determinants of exercise intentions in Multiple Myeloma. *Cancer Nursing, 29*(3), 167-175.

Jones, L. W., Guill, B., Keir, S. T., Carter, K., Friedman, H. S., Bigner, C. D., . . . Reardon, D. A. (2007). Using the theory of planned behavior to understand the determinants of exercise intention in patients diagnosed with primary brain cancer. *Psycho-oncology, 16,* 232-240.

Karvinen, K. H., Courneya, K. S., Campbell, K. L., Pearacey, R. G., Dundas, G., Capstick, V., & Tonkin, K. (2007). Correlates of exercise motivation in a population-based sample of endometrial cancer survivors: An application of the Theory of Planned Behavior. *International Journal of Behavioral Nutrition and Physical Activity, 4,* 21.

Kim, S., & Kim, H. S. (2006). A series of bed exercises to improve lymphocyte count in allogeneic bone marrow transplantation patients. *European Journal of Cancer Care—English Version, 15,* 453-457.

McNeely, M. L., Parliament, M. B., Seikaly, H., Jha, N., Magee, D. J., Haykowsky, M. J., & Courneya, K. S. (2012). Predictors of adherence to an exercise program for shoulder pain and dysfunction in head and neck cancer survivors. *Supportive Care Cancer, 20,* 515-522.

Mello, M., Tanaka, C., & Dulley, F. L. (2003). Effects of an exercise program on muscle performance in patients undergoing allogeneic bone marrow transplantation. *Bone Marrow Transplant, 32,* 723-728.

Milne, H. M., Wallman, K. E., Guifoyle, A., Gordon, S., & Courneya, K. S. (2008). Self-determination theory and physical activity among breast cancer survivors. *Journal of Sport Exercise Psychology, 30*(1), 23-28.

Peddle, C. J., Jones, L. S., Eves, N. D., Reiman, T., Sellar, C. M. Winton, T., & Courneya, K. S. (2009). Correlates of adherence to supervised exercise in patients awaiting surgical removal of malignant lung lesions: Results of a pilot study. *Oncology Nurse Forum, 36*(3), 287-295.

Rogers, L. Q., Markwell, S., Hopkins-Price, P., Vicari, S., Courneya, K. S., Hoelzer, K., & Verhulst, S. (2011). Reduced barriers mediated physical activity maintenance among breast cancer survivors. *Journal of Exercise Psychology, 33*(2), 235-254.

Vallance, J. K. H., Courneya, K. S., Jones, L. W., & Reiman, T. (2006). Exercise preferences among a population-based sample of non-Hodgkin's lymphoma survivors. *European Journal of Cancer Care, 15,* 34-43.

White, A., Miller, K. B., & Ryan, H. F. (2005). Impaired respiratory and skeletal muscle strength in patients prior to hematopoietic stem cell transplantation. *Chest, 128,* 145-152.

Wilson, R., Jacobsen, P. B., & Fields, K. K. (2005). Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. *Bone Marrow Transplant*, *35*, 721-727.

Wilson, P. M., Blanchard, C., Nehl, E., & Baker, F. (2006). Predicting physical activity and outcome expectations in cancer survivors: An application of self-determination theory. *Psycho-oncology, 15*(7), 567-578.

World Cancer Research Fund & American Institute for Cancer Research. (2007). *Food, nutrition, physical activity and the prevention of cancer: A global perspective. Physical activity*. Washington, DC: American Institute for Cancer Research

CHAPTER 5

DISCUSSION

Introduction

There are approximately 50,000 hematopoietic stem cell transplants (HSCT) performed worldwide each year (Gratwohl et al., 2010). Improvements in stem cell transplant technology and supportive after care have allowed for increased survival rates. Pre transplant status is often compromised in a substantial number of patients prior to treatment secondary to inactivity, side effects from medications, chemo-therapy, or the disease itself. Respiratory, skeletal muscle strength and maximal exercise capacity is reduced (White, Miller, & Ryan, 2005) making recovery of physical function even more demanding. Approximately 40-50% of patients continue to experience physical, psychological, and psychosocial stress up to 5 or more years after transplant (Bhatia et al., 2007). With mortality rates twice as high as that of the general population (Bhatia et al., 2007), these patients continue to survive with many issues that impact their health and quality of life.

There is increasing evidence that demonstrates that participation in regular physical exercise during and after HSCT treatment can improve or, at a minimum, stabilize the effects of treatment. The research that has been completed is limited by lack of randomization, small sample size, and heterogeneity of settings. This has limited the translation into clinical practice. Additionally, there remains no consensus as to type or dose of activity or factors and approach that predict adoption and adherence of exercise in hematopoietic stem cell transplant patients. Improved knowledge in this area of research has the potential to (a) strengthen supportive care for individuals undergoing stem cell transplant, (b) clarify type and dose of activity that is optimal, and (c) aid in the development of strategies to increase adherence to exercise.

The objectives of this study were to (a) determine the feasibility (recruitment, adherence and attrition) of an exercise intervention versus an attention control group, and (b) examine the relationship between the exercise intervention and control on function, fatigue, perceived exertion, muscular strength, and cardiopulmonary status. A third aim explored the relationship of attitude, intention to exercise, subjective norms and perceived behavioral control and their contribution to variance in exercise behavior (based on the theory of planned behavior (Azjen & Driver, 1992).

Sample

The sample (*N* = 60) for this experimental, repeated measures design study was a convenience sample taken from approximately 340 adult stem cell transplant patients that are seen annually. All participants were adults who were deemed eligible for stem cell transplant by their hematologist for hematologic malignancies. They were recruited to the study either by self-referral or were referred by providers at the clinic where they were being treated. Participants were a median age of 53.6 (range 19-71) years and primarily Caucasian (*n* = 58; 96%). Ninety percent had undergone an autologous stem cell transplant with 10% receiving stem cells or bone marrow from a matched sibling or unrelated donor. Participants were involved in the study from the time they initiated stem cell collection (if applicable) through the recovery of their white count (absolute neutrophil count of 0.5 for 3 consecutive days or 1.0 for one day).

Summary of Results

The first aim of this study was to test for feasibility, adherence, recruitment rate and attrition. Sixty participants consented and completed the study out of 72 patients approached. Average behavioral adherence for the control group was 69.3% and 79.6% for the exercise group. This percentage of adherence reflects the days that participants were eligible to exercise and chose to do so. These percentages for the control group reflect the number of days they attended scheduled classes. There was no attrition.

The second aim examined the relationship between the exercise intervention versus the attention control group on functional capacity as measured by the Functional Performance Inventory (Leidy, 1999); fatigue as measured by the Schwartz Cancer Fatigue Scale (Schwartz, 1998); perceived exertion (Borg Scale; Borg, 1998); muscular strength as measured by the grip strength and the step ascent test; and cardiopulmonary status which was measured by the 6-minute walk. Exercise activity both completed in the study as well as outside the study was captured weekly using the Godin Leisure Time Questionnaire (Godin & Shepard, 1985).

Functional performance which was measured at baseline, weeks 1, 2, 3, 4, and post study showed a significantly positive difference for the intervention group (p = .041). Similarly, fatigue which was also measured at baseline, weeks 1, 2, 3, 4, and post study showed significance for the intervention group (p = .041). Across time, fatigue scores remained relatively stable for the intervention group; however; they increased for the control group. Since increased scores indicate increased fatigue, this finding suggests that exercise provided a stabilization effect for the intervention group while participants in the control group experienced more fatigue.

This study utilized two measures of strength. Although the grip strength test was not statistically significant (p = .072), at baseline and post testing, the intervention group lost 2.74 kilograms while the control group lost 6.11 kilograms. While both groups lost grip strength, the intervention group lost less than the control group. This again, suggests a stabilization or reduced loss of strength for the intervention group. The other measure used to test strength was the step ascent test. The mean step ascent test scores (measured in seconds) at baseline and post were significantly significant for the intervention group (p = < .001) with improved strength for that group. The control group lost strength and took significantly longer to climb the flight of stairs when compared to the intervention group.

Cardiopulmonary status or endurance as measured by the 6-Minute Walk was statistically improved for the intervention group (p = .001). Overall, cardiopulmonary scores deceased from baseline to posttest. The control group showed more of a decline when compared to the intervention group.

Taken together, these results further validate preliminary research that says exercise is safe and feasible for a unique population of patients undergoing challenging medical treatment such as stem cell transplantation. A unique contribution is the inclusion of both allogeneic and autologous transplant patients during the active treatment phase. Only one other study to date has done so during the course of treatment with both transplant types (Baumann, Kraut, Schule, Bloch, & Fauser, 2010). This is a period when many patients are experiencing significant side effects from chemo-therapy including nausea, diarrhea, diminished nutritional intake, and pancytopenia. Allogeneic patients typically have more side effects and complications in the treatment phase and in the immediate recovery period. Our study supports the idea that a controlled exercise program right from the beginning of the conditioning phase can contribute positively to function, strength and lessen their fatigue.

Behavioral adherence to exercise in this study was 79.63% for the intervention group. Participants in the intervention group were not allowed to participate if they were thrombocytopenic (platelet count 20,000 or less), orthostatic (subjectively light headed or dizzy), febrile or not did feel well enough to exercise that day. The reported adherence for the intervention group reflects this.

Our adherence was not as significant as other supervised studies. Average compliance rates across studies are reported to be approximately 85% (Wiskemann & Huber, 2008). As could be expected, the rate for home-based (not supervised) is below the average 68% whereas the supervised studies (in/out patient) are approximately 90%. Our study was based primarily in an out-patient setting while the majority of previous supervised exercise studies took place while participants \were hospitalized. Our study also took place during the active treatment phase. In our study participants only missed for medical reasons and still gained benefit in maintenance of fitness and decreasing symptoms such as fatigue.

Average compliance rates across studies are reported to be approximately 85% (Wiskemann & Huber, 2008). As could be expected, the rate for home-based (not-supervised) is below that average (68%) whereas the supervised settings (in/out patient) are approximately 90%. Many of these studies were not completed during active treatment so this impacts adherence rates.

Aim two also examined endurance and aerobic fitness. This was the most common kind of exercise intervention in previous studies. The research shows mixed results with exercise studies that took place in the hospital setting and during active treatment. Dimeo, Fetscher, Lnaage, Mertelsmann, and Keul (1997), using the inpatient model showed that regular endurance training may not lead to an increase in endurance performance, but the loss of performance in the experimental group was significantly lower than in associated control group ($p < 0.01$). Another study showed that an increase of physical performance via endurance training cannot be achieved during the hospitalization stay (Baumann, Schule, Fauser, & Kraut, 2005). This was also shown in one uncontrolled study (Dimeo et al., 1996). Baumann et al. (2010), also with an inpatient model showed an advantage for the intervention group with endurance. They, similarly to this current study, included both autologous and allogeneic participants and also provided the exercise intervention during actual treatment and the immediate recovery period. Baumann et al. (2010) found that the endurance performance of their treatment group remained nearly unchanged during the training period while that of the control group decreased quite substantially (with a difference in endurance testing by 27%). Our study's results also show a significant advantage for the intervention group with endurance. Our study also included both transplant types and occurred during the active treatment phase but took place in the out-patient setting, showing that patients were able to adhere to a supervised exercise program during active treatment.

While the majority of the research with exercise and stem cell transplant patients has used endurance training, there is additional evidence to support the use of both endurance and resistance training. Our study included both resistance and endurance training based on recommendations from the American College of Sports Medicine and shows additional support for the inclusion of both types of exercise training. Hayes, Davies, Parker, Bashford, and Green (2004) and Mello, Tanaka, and Dulley (2003) found that, in the context of their similarly out-patient exercise intervention, patients benefitted from the applied resistance training. Mello et al. (2003) with their combined in and outpatient intervention strategy only showed a stabilization effect of resistance training concerning different muscle groups in the experimental group. Our study supports research stating that the inclusion of both endurance and resistance training in future research is optimal to targeting the type and dose of physical activity for stem cell transplant patients.

A concern in research with exercise and stem cell transplant patients is not only the type of exercise that is most beneficial but the dose of activity. The participants in this study were able to exercise at a moderate perceived exertion level throughout their participation. Looking at the average perceived exertion (Borg Scale of Perceived Exertion 1-10), scores for the six collection time points, both groups were able to exercise at a moderate level with an average of 3.63 for the control group and 3.23 for the intervention group. Scores of 3-4 are considered moderate to somewhat strong (Borg, 1982). This suggests that stem cell transplant patients can exercise at moderate levels at the active phase of treatment and provides some guidance on the dose of activity that may help guide future research.

This study was based on a theoretical framework, the Theory of Planned Behavior (Azjen & Driver, 1992). Aim three of our study examined the tenets of attitude, perceived behavioral control, subjective norms, and intention to exercise. This aim was examined by multiple regression. A pre- and postexercise change score was entered into the equation and then tested against the four predictor variables, attitude towards exercise, intention to exercise, subjective norms and perceived behavioral control. The model as a whole was found to account for 20.3% of the variance in exercise behavioral. Perceived behavioral control and intention trended towards significance and may be determinants to be explored in future research. The examination of variables that contribute to adherence in physical activity adds to previous research indicating that the correlates of the Theory of Planned Behavior will provide a useful framework on which to base interventions designed to increase exercise intentions in HSCT survivors. The inclusion of a theoretical framework in the research of exercise with HSCT patients is unique and adds an important dimension for the adoption and maintenance of exercise activity. Three previous studies have examined the determinants of exercise behavior (Courneya, Keats, & Turner, 2000; Courneya, Vallance, Jones, & Reiman, 2005; Jones et al., 2006) in this population. Our study did not look at demographic, medical variables and social-cognitive determinants as possible predictors; however, Jones et al. did not find that these variables had any association between the theory of planned behavior and exercise intention.

Intention and perceived behavioral control were found to be key predictors of the variance in exercise behavior in our study. This is consistent with the general literature on the theory of planned behavior and exercise (Godin & Kok, 1996). In several prospective studies by Courneya (Courneya, Friedenreich, Arthue, & Bobick,1999; Courneya et al., 2000; Courneya, Blanchard, & Laing, 2001) exercise intention explained significant variance in behavior of exercise in breast cancer survivors (30%), bone marrow transplant survivors during treatment (36%) and colorectal survivors also during treatment (30%). Azjen and Driver (1992) postulated that intention was the proximal determinant of behavior. In our study, intention, while not statistically significant, was a potentially meaningful determinant of exercise behavior. One might speculate that in the presence of favorable intention along with perceived behavioral control, future investigators and clinicians could enhance feelings of intention and control. Notwithstanding, the small sample size in this study, the correlation of intention and perceived behavioral control may portend to the unique motivations of stem cell transplant patients. Patients often come to transplant knowing that they face many weeks and months of recovery. They are faced with many physical and psychosocial stressors and may not feel in control of their ability to engage in physical activity. However, once they know that they can exercise; they may be more apt to believe that the ability to exercise is in their control. From a practical perspective, it appears that structured interventions reinforcing perceptions of control could influence intentions to exercise duration active treatment.

Several more recent studies by Courneya et al. (2005) and Jones et al. (2006) found that attitude provided a unique contribution to exercise variance. Similar to an earlier study by Courneya et al. (2000), attitude was not found to be significant in our study (p = .92). The participants in the 2000 Courneya study, as in the current study, took place during actual treatment and in the immediate recovery period. One possible explanation may be the different cancer populations being investigated. Another possible explanation is that patients undergoing challenging treatments may have additional concomitant co morbidities and may be experiencing more treatment related side effects. The benefits of exercise may not be as readily accepted at that stage in their treatment and they may not have a positive attitude towards physical activity. However, if exercise is incorporated into active treatment, patients may be willing to participate as part of their recovery even though they do not have a positive attitude towards exercise itself. Future trials testing the effects of exercise training may want to include variability in diagnoses and treatment trajectory.

While overall, the Theory of Planned Behavior shows promise as a framework to understand the variables that contribute to exercise behavior, there remains variability in the findings. This highlights the importance of conducting theoretically based research before designing and implementing behavior interventions designed to promote general exercise levels or maximize adherence to a training intervention. It is possible that the performance of theoretically based research at different stages across the transplant experience may provide more effective guidance for the clinician and aid in the development of interventions to enhance behavioral adoption and adherence to exercise.

Limitations

Several caveats must be considered in interpreting the results of these analyses. First, the data were collected at a single center. Individuals seen at this site may not represent the transplant population in terms of types of transplant done, specific indications for transplant, and lastly, other centers may use different criteria for accepting a patient for stem cell transplantation. While this study's participants reflected the ethnicity of the catchment area, it did not reflect national ethnicity profiles of the represented diagnoses in the general transplant population.

The sample size was relatively small although it compares favorably with other studies with HSCT patients. While it shows the feasibility and safety of exercise training during the treatment phase and immediate recovery, it did not follow patients beyond that period. This limits the value of the information gained regarding adherence variables. Since we know that these patients continue to struggle with dysfunction up to a year or more posttransplant (Bhatia et al., 2007), it would be helpful to know how many participants adopted exercise behavior and made life style changes after the initial recovery.

While it is a strength of this study that we controlled for age, gender, and socio-economic status and exercise history, we did not examine diagnoses or specified differences between allogeneic and autologous transplant types as we did not have adequate sample size to do so. We also had more allogeneic transplants in the intervention group so the randomization schema failed to balance the assignment of the type of transplant and may be a factor in differences between groups. This was controlled for on the analysis and we still had superior results with participants that typically would experience more side effects of treatment which would preclude them to be unable to attend. Examination of diagnoses and type of transplant may guide the development of future interventions and provide additional data to guide the individualization of exercise training into clinical nursing practice.

Both groups were run by the primary investigator. This may have introduced a level of bias. The primary investigator was aware of the fact that unintended bias could be operational in a comparison study totally run by the investigator where no blinding was possible. Therefore, at all stages of this research, including recruitment, the actual intervention, the attentional control condition, data collection for both groups, and analysis the investigator strove for objectivity.

Another limitation is the possibility of the development of cross- contamination between groups. Many of these patients resided in the same housing and could interact in reception areas and while receiving medical care. There may have been some cross-contamination of the two groups such as compensatory rivalry or resentful demoralization. However, examination of the data does not reflect significant differences between the groups on leisure time exercise or rate of nonadherence to assigned group participation or personal effort on outcome measures.

An additional limitation is the self-report assessment of exercise behavior. Although those participating in the intervention arm were directly observed, any additional exercise completed outside the study by either group was self report. Future research might use objective activity monitors (i.e., pedometers) or only supervised exercise training to verify exercise behavior.

While acknowledging how these limitations may have affected the outcomes, this study is one of two that have prospectively included both allogeneic and autologous stem cell transplant patients in a randomized and controlled study during the active treatment phase. It is one of the first to include a theoretical framework to examine determinants of exercise intention. These strengths contribute to the development of a larger multicenter randomized clinical trial.

Recommendations for Future Research

The results of this study suggest a number of implications for future research. As an initial step, replication of this study with a larger and more heterogeneous population of diagnoses and transplant types is necessary to define type and dose of exercise. Our study suggests that endurance and strength training hold potential for effective exercise training in both types of transplants during the active treatment phase. Research is needed to develop and refine interventions. Multidisciplinary collaboration with nursing, physical therapy, and medicine could provide additional input into not only the research but the ultimate translation into practice. Increasing the interplay between disciplines would likely lead to improved treatment and therapy results. For example, the two evidence-based practices of physical therapy paired with psychosocial interventions could be used for a behavioral therapy approach to symptoms and functionings (Mundy, DuHamel, & Montgomery, 2003; Redd, Montgomery, & DuHamel, 2001). For example, the combination of stress reduction and exercise training with the method of mindfulness-based stress reduction based on Jon Kabat-Zinn might be considered and might be a useful approach for patients undergoing challenging therapies such as HSCT (Ott, Norris, & Bauer-Wu, 2006; Smith, Richardson, Hoffman, & Pilkington, 2005)

There is a need for long term follow-up with this population particularly since we know that many continue to struggle with significant deconditioning and impaired quality of life (Bhatia et al., 2007). It is established that exercise is safe and feasible in this population but we do not know definitively the type or dose of exercise that is optimal for patients in the various trajectories of recovery. Further, we do not fully understand the determinants of exercise behavior at various stages throughout the transplant experience.

Building interventions based on theoretical models such as the theory of planned behavior, which was shown to be predictive of exercise in our study, could encourage the development of guidelines to increase exercise adherence.

Recommendations for Clinical Practice

The results of this study add to our understanding that exercise in the HSCT population is beneficial. To better understand how physical activity can impact an HSCT patient's treatment and recovery, there is a need for a more systematic assessment of how patients might successfully integrate physical activity into their daily lives. A finding in the exercise literature is that past exercise behavior was important for understanding future exercise behavior beyond the theory of planned behavior (Godin & Kok, 1996). Nursing is in a unique position to work towards the integration of such assessments in their hospital admission assessments and on-going out-patient services. Assessments for flexibility, endurance, and strength can easily be included with focused physical exams. Inquiring about what types of activities patients are engaged in, past and present, could provide unique opportunities to encourage, support, and educate patients about the benefits of physical activity.

Medical progress in recent years for long-term survival for HSCT patients increases the urgency to incorporate interventions that counter debilitating impact of the disease and its treatment. Currently, rehabilitation is withheld until the posttransplant phase. Physical therapy is typically reserved for patients that are so severely deconditioned that they require total physical assistance from nursing staff. This study contributes to understanding the value of exercise during active treatment in preventing further deconditioning. To avoid these consequences, exercise therapy should be offered to patients right from the beginning of the acute phase of therapy and onward. Again, nursing is in a key position to facilitate and encourage adherence to exercise during treatment. The development of supportive guidelines that can be integrated into nursing care plans would aid in the support of patients to engage in exercise training to actively maintain and improve function and quality of life.

The development of strategies that aid with adoption and adherence of physical exercise is equally suited to the nursing profession as nurses often have more direct contact with patients in their day-to-day recovery. As longer term follow-up and supportive care become a reality, technology such as videoconferencing and other telehealth strategies might be utilized to track adherence, provide support and additional information regarding the development of exercise training programs that would meet the individual needs.

Summary

This study adds to the body of knowledge in this area in three important ways. One, this study engaged both allogeneic and autologous patients prior to receipt of chemotherapy and through their immediate recovery. Only one study to date has utilized both transplant types during this treatment phase and the immediate transplant recovery (Baumann et al., 2010). This is a period when patients are experiencing side effects from chemotherapy including nausea, diarrhea, diminished nutritional intake and pancytopenia.

Second, this study contributes to a growing body of knowledge that shows that exercise should be included in recovery planning. In a 2010 editorial in *Bone Marrow Transplant* (Somerfield & Rizzo, 2010), Doctors Somerfield and Rizzo from the Cancer

Policy and Clinical Affairs of the American Society of Clinical Oncology and The Center on International Blood and Marrow Transplant Research, respectively, called for additional research in this area. They recommended a larger randomized multi-center controlled trial to address the methodological problems with previous studies and that could determine whether or not an exercise program in the early period of transplantation improves quality of life and physical functioning. This study contributes preliminary evidence for a larger multisite trial. This study also provides additional information about the type and intensity of exercise that these patients can engage in during immediate recovery. This is important for the development of rehabilitation programs for this population. Multiple efforts now exist to increase the capacity of fitness professionals, including nurses and physical therapists, to serve the needs of stem cell l transplant and cancer patients in general (Schmitz et al., 2010).

Third, this study evaluated the predictive value of a theoretical framework, the Theory of Planned Behavior (Azjen & Driver, 1992). By studying how attitudes, intention, subjective norms, and perceived behavioral control influence exercise behavior we gain insights that are useful in assisting patients to adopt and maintain physical activity. If included in future research, we can consider the integration of these concepts into the development of an individualized rehabilitation program for stem cell transplant patients.

In summary, this study provides further support for the use of exercise training as part of the management of stem cell transplant survivors. It provides evidence that exercise is beneficial at a time when many patients are not expected to engage in such activities. Additional information about the type, timing, and dose of exercise will be useful for future research as well the development of rehabilitation programs and fitness professionals. Lastly, gained insights in predictive variables such as intention and perceived behavioral control can be applied to the adoption and maintenance of healthy behaviors and the development of supportive care guidelines for the on-going recovery of stem cell transplant patients.

References

Ajzen, I., & Driver, B. L. (1992). Application of planned behavior to leisure choice. *Journal of Leisure and Rest, 24*(3), 207-224.

Baumann, F.T., Kraut, L., Schule, K., Bloch, W., & Fauser, A. A. (2010). A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplantation, 45*, 355-362.

Baumann, F. T., Schule, K., Fauser, A. A., & Kraut, L. (2005). The effects of exercise therapy after stem cell transplantation. *German Journal of Oncology, 37,* 152-158.

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker, S., Gurney, J. G., . . . Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: Report from the Bone Marrow Transplant Survivor Study. *Blood*, *110*(10), 3787-3792.

Borg, G. (1982). Psychological basis of perceived exertion. *Medicine and Science in Sports and Exercise, 14,* 337-381.

Borg, G. (1998). *Borg's perceived exertion and pain*. Champaign, IL: Human Kinetics.

Courneya, K., Blanchard, C. M., & Laing, D. (2001). Exercise adherence in breast cancer survivors training for a dragon boat race competition: A preliminary investigation. *Psycho-oncology, 10,* 444-452.

Courneya, K., Friedenreich, C. M., Arthue, K., & Bobick, T. M. (1999). Understanding exercise motivation in colorectal patients: A prospective study using the theory of planned behavior. *Rehabilitation Psychology, 44*(1), 68-84.

Courneya, K., Keats, M. R., & Turner, A. R. (2000). Social cognitive determinants of hospital-based exercise in cancer patients following high dose chemotherapy and bone marrow transplantation. *International Journal of Behavioral Medicine, 7*(3), 189-203.

Courneya, K., Vallance, J. K. H., Jones, L. W., & Reiman, T. (2005) Correlates of exercise intentions in non-Hodgkin's lymphoma survivors: An application of the theory of planned behavior. *Journal of Sports Medicine Psychology*; 27: 335-347.

Dimeo, F., Bertz, H., Finke, J., Fetscher, S., Mertelsmann, R., & Keul, J. (1996). An aerobic exercise program for patients with haematological malignancies after bone marrow transplantation. *Bone Marrow Transplant, 18,* 1157-1160.

Dimeo, F., Fetscher, S., Lnaage, W., Mertelsmann, R., & Keul, J.. (1997). Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood*, *90*, 3390-3394.

Godin, G., & Kok, G. (1996). The theory of planned behavior: A review of its application to health-related behaviors. *American Journal of Health Promotion, 11,* 87-98.

Godin, G., & Shepard, R. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Sciences, 10*(3), 141-146.

Gratwohl, A., Baldomero, H., Aljurf, M., Pasquini, M. C., Bouzas, L. F., Yoshimi, A., . . . Kodera, Y. (2010). Hematopoietic stem cell transplantation: A global perspective. *Journal of the American Medical Association*, *303*(16, 1617-1624.

Hayes, S., Davies, P. S., Parker, T., Bashford, J., & Green, A. (2004). Role of a mixed-type, moderate intensity exercise programme after peripheral blood stem cell transplantation. *British Journal of Sports Medicine, 38*, 304-309.

Jones, L., Courneya, K. S., Vallanec, J. K., Ladha, A. B., Mant, M. J., Belch, A. R., & Reiman, T. (2006). Understanding the determinants of exercise intentions in Multiple Myeloma. *Cancer Nursing, 29*(3), 167-175.

Leidy, N. K. (1999). Psychometric properties of the functional performance inventory in patients with chronic obstructive pulmonary disease. *Nursing Research, 48*(1), 20-28.

Mello, M., Tanaka, C., & Dulley, F. L. (2003). Effects of an exercise program on muscle performance in patients undergoing allogeneic bone marrow transplantation. *Bone Marrow Transplant, 32*, 723-728.

Mundy, E. A., DuHamel, K. N., & Montgomery, G. H. (2003). The efficacy of behavioral interventions for cancer treatment-related side effects. *Seminars in Clinical Neuropsychiatry*, *8,* 253-275

Ott, M. J., Norris, R. L., & Bauer-Wu, S. M. (2006). Mindfulness mediation for oncology patients: A discussion and critical review. *Integrative Cancer Therapies,* 5, 98-108.

Redd, W. H., Montgomery, G. H., & DuHamel, K. N. (2001). Behavioral intervention for cancer treatment side effects. *Journal of National Cancer Institute, 93,* 810-823.

Schmitz, L. H., Courneya, K. S., Matthews, C., Demark-Wahnefried, W., Galvao, D. A., Pinto, B. M, . . . Schwartz, A. (2010). American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Medicine & Science in Sports and Exercise, 42*, 1409–1426.

Schwartz, A. I. (1998). The Schwartz Cancer Fatigue Scale: Testing, reliability and validity. *Oncology Nursing Forum, 25*(4), 717-722.

Smith, J. E., Richardson, J., Hoffman, C., & Pilkington, K. (2005). Mindfulness-based stress reduction as supportive therapy in cancer care: A systematic review. *Journal of Advanced Nursing, 52*, 315-327.

Somerfield, M. R., & Rizzo. J. D. (2010). Can a modest exercise program really improve physical functioning and quality of life among recipients of hematopoietic SCT? *Bone Marrow Transplant, 45*(2), 217-218.

White, A., Miller, K. B., & Ryan, H, F. (2005). Impaired respiratory and skeletal muscle strength in patients prior to hematopoietic stem cell transplantation. *Chest, 128*, 145-152.

Wilson, R., Jacobsen, P. B., & Fields, K, K. (2005). Pilot study of a home-based aerobic exercise program for sedentary cancer survivors treated with hematopoietic stem cell transplantation. *Bone Marrow Transplant, 35*, 721-727.

Wiskemann, J., & Huber, G. (2008). Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant, 41*, 321-329.

APPENDIX A

FUNCTIONAL PERFORMANCE INVENTORY—SHORT FORM

Functional Performance Inventory—Short Form

This questionnaire asks about how your health usually affects your day-day activities. Please circle the number that best describes how difficult it is for you, in general, to do the following activities. Circling 1 means you do the activity easily, with no difficulty at all, 2 means you do it with some difficulty, 3 means you have much difficulty, and 4 means you no longer do this activity because of your health. If you have never done, or choose not to do, an activity for reasons other than your health, please circle n/a (not applicable).

	DO with…			DON'T DO because…	
	No Difficulty	Some Difficulty	Much Difficulty	Health Reasons	Choose Not To
Body Care					
dressing & undressing	1	2	3	4	n/a
showering or bathing	1	2	3	4	n/a
caring for your feet	1	2	3	4	n/a
washing your hair	1	2	3	4	n/a
shaving or applying makeup	1	2	3	4	n/a
Maintaining the Household					
groceries & meals:					
preparing meals/cooking	1	2	3	4	n/a
grocery shopping	1	2	3	4	n/a
carrying groceries	1	2	3	4	n/a
activities around the house or apartment, such as:					
vacuuming or sweeping	1	2	3	4	n/a
moving furniture, changing sheets, or washing windows	1	2	3	4	n/a
cleaning bathrooms or washing floors	1	2	3	4	n/a
moving the lawn, shoveling snow, raking, or heavy gardening	1	2	3	4	n/a
going to appointments (such as doctors or dentists	1	2	3	4	n/a
Physical Exercise					
regular stretching, moving, or lifting light weights	1	2	3	4	n/a
walking up and down a flight of stairs	1	2	3	4	n/a
short walks around the neighborhood or mall	1	2	3	4	n/a
long fast walks (more than 20 minutes)	1	2	3	4	n/a
activities such as swimming or bicycling	1	2	3	4	n/a

Please continue to the next page.

Remember, if you have never done, or choose not to do, an activity for reasons other than your health, please circle n/a (not applicable).

	DO with…			DON'T DO because…	
	No Difficulty	Some Difficulty	Much Difficulty	Health Reasons	Choose Not To
Recreation—activities for personal pleasure					
taking vacations	1	2	3	4	n/a
activities away from the house or apartment					
indoor activities such as shopping or museums..............................	1	2	3	4	n/a
going to the movies	1	2	3	4	n/a
activities in and around the house or apartment					
sitting outside	1	2	3	4	n/a
reading..	1	2	3	4	n/a
Spiritual Activities					
attending religious services..............	1	2	3	4	n/a
going to religious ceremonies	1	2	3	4	n/a
personal reading, meditation, or prayer	1	2	3	4	n/a
visits from spiritual friends or teachers	1	2	3	4	n/a
Social Interaction—family and friends					
dinner, cards, bingo or other activity in your home...............................	1	2	3	4	n/a
places other than your home					
helping family or friends: going to the store, giving rides, doing repairs or other favors.....	1	2	3	4	n/a
helping in the care of children	1	2	3	4	n/a
distant or overnight travel to visit others	1	2	3	4	n/a

.

APPENDIX B

SCHWARTZ CANCER FATIGUE SCALE

Schwartz Cancer Fatigue Scale

The words and phrases below describe different feelings people associate with fatigue. Please read each item and circle the number that indicates how much fatigue has made you feel in the past 2-3 days.

1 = not at all
2 = a little
3 = moderately
4 = quite a bit
5 = extremely

Tired	1 2 3 4 5
Difficulty thinking	1 2 3 4 5
Overcome	1 2 3 4 5
Listless	1 2 3 4 5
Worn out	1 2 3 4 5
Helpless	1 2 3 4 5

APPENDIX C

BORG PERCEIVED EXERTION SCALE

Borg Perceived Exertion Scale

How to use the Perceived Exertion Scale

While doing physical activity, we want you to rate your perception of exertion. This feeling should reflect how heavy and strenuous the exercise feels to you, combining all sensations and feelings of physical stress, effort, and fatigue. Do not concern yourself with any one factor such as leg pain or shortness of breath, but try to focus on your total feeling of exertion.

Look at the rating scale below while you are engaging in an activity; it ranges from 6 to 20, where 6 means “no exertion at all” and 20 means “maximal exertion.” Choose the number from below that best describes your level of exertion. This will give you a good idea of the intensity level of your activity, and you can use this information to speed up or show down your movements to reach your desired range.

Try to appraise your feeling of exertion as honestly as possible, without thinking about what the actual physical goal is. Your own feeling of effort and exertion is important, not how it compares to other people’s. Look at the scales and the expressions and then give a number.

6	No exertion at all
7	Extremely light
8	
9	Very light (easy walking slowly at a comfortable pace)
10	
11	Light
12	
13	Somewhat hard (it is quite an effort; you feel tired but can continue)
14	
15	Hard (heavy)
16	
17	Very hard (very strenuous, and you are very fatigued)
18	
19	Extremely hard (you cannot continue for long at this pace)
20	Maximal exertion

APPENDIX D

6-MINUTE WALK TEST INSTRUCTIONS

6 Minute Walk Test Instructions

General Information

Individual walks without physical assistance for 6 minutes and the distance is measured

Start timing when the individual is instructed to "Go"

Stop timing at 6 minutes

Assistive devices can be used but should be kept consistent and documented from test to test

If physical assistance is required to walk, this should not be performed

A measuring wheel is helpful to determine distance walked

Should be performed at the fastest speed possible

Set-up and Equipment

Ensure the hallway free of obstacles

Stopwatch

Measuring wheel recommended to calculate distance

Patient instructions (derived from references below):

"Cover as much ground as possible over 6 minutes. Walk continuously if possible, but do not be concerned if you need to slow down or stop to rest. The goal is to feel at the end of the test that more ground could not have been covered in the 6 minutes."

References:

Butland, RJ, Pang J, Gross ER, Woodcock AA, Gesses DM. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J (Clin Res Ed).* 1982 May 29; 284(6329):1607-8.

McGavin, CR, Gupta SP, McHardy GJ. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J.* 1976; 3;1(6013):822-3.

Rossier, P, Wade DT. Validity and reliability comparison of 4 mobility measures in patients presenting with neurologic impairment. *Arch Phys Med Rehabil.* 2001:82(1):9-13.

6 Minute Walk Test

Name: ____

Date: ______________________

Distance ambulated in 6 minutes: ___________________

Date: ______________

Distance ambulated in 6 minutes: ___________________

Date: ______________

Distance ambulated in 6 minutes: ___________________

Date: ______________

Distance ambulated in 6 minutes: ___________________

Date: ______________

APPENDIX E

GRIP STRENGTH

Grip Strength

Materials needed:

Chair

Hand dynamometer (adult or child)

Procedure:

A. Patient sits in chair, arms unsupported
B. Instruct patient to squeeze dynamometer as hard as they can with dominant hand
C. Repeat for a total of 3 times, recording each result
D. Average the three results and record the grip strength in pounds per square inch.

APPENDIX F

RECRUITMENT FLYER

MAYO CLINIC

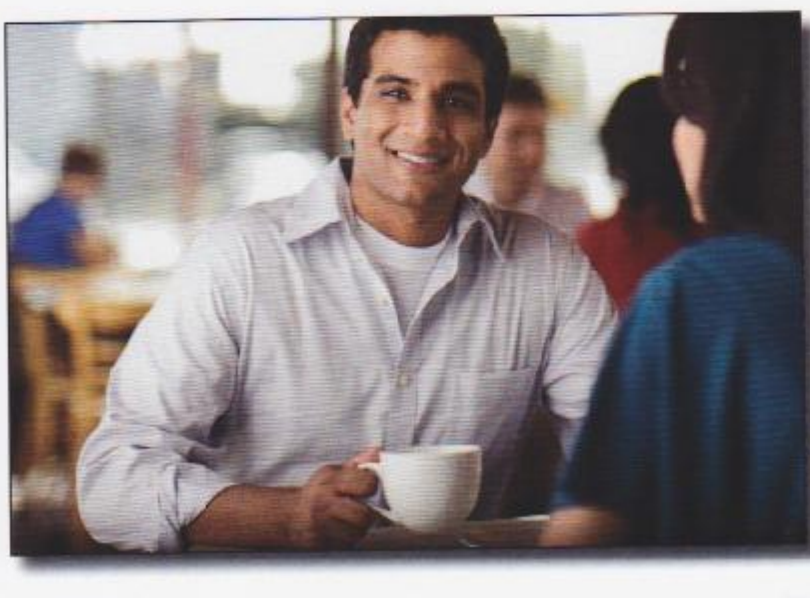
Stem Cell Transplant Patients Needed for Research Study

Mayo Clinic is seeking stem cell transplant patients for a research study. The purpose of this study is to learn how exercise affects someone receiving a bone marrow transplant.

You may be eligible to participate if:
- You are between 18 and 65 years old.
- You are scheduled to receive a bone marrow transplant.
- Your hematologist recommended you for this study.

If you agree to participate, you will be in this study for several weeks. You will be randomly assigned to 1 of 2 groups. One group will participate in group exercise activities 3 times a week. The other group will also meet 3 times a week to learn about health-related topics, but they but will not participate in exercise activities a a group. Remuneration will not be offered.

For more information, contact Randi Hoffmann at (507) 266-7504 or Hoffmann.randi@mayo.edu.



APPENDIX G

DEMOGRAPHIC FORM

Demographic Form

Identifying number ______________________

1. Are you:

Male ☐ Female ☐

2. What is your age:

☐ 18-24 ☐ 25-34

☐ 35-44 ☐ 45-54

☐ 55-64 ☐ 65 or over

3. What is the highest level of formal education you have completed?

☐ Attended high school ☐ Graduated high school

☐Attended college ☐ Graduated college

☐ Post graduate study without degree ☐ Post graduate degree

4. What is your marital status?

☐ Married ☐ Single–never-married

☐ Separated–divorced ☐ Widowed

5. What is your ethnic group?

☐ Hispanic ☐ African American

☐ Asian ☐ Native American

☐ White/Caucasian ☐ Pacific Islander

☐ Other-please identify ________________________________

6. Employment:

☐ Full time ☐ Part-time ☐ Unemployed ☐ Disabled ☐ Retired

7. What is your total household annual income? Please include income for all family members and all sources such as salary, investment, rents, royalties, etc.)

☐ Less than $30,000 ☐ $30,000-$39,999

☐ $40,000-$49,000 ☐ $50,000-$59,999

☐ $60,000-$74,999 ☐ $75,000-$99,999

☐ $100,000-$149,000 ☐ $150,000-$249,999

☐ $250,000 or more

APPENDIX H

GODIN LEISURE TIME EXERCISE QUESTIONNAIRE

Godin Leisure-Time Exercise Questionnaire

Instructions

In this excerpt from the Godin Leisure-Time Exercise Questionnaire, the individual is asked to complete a self-explanatory, brief four-item query of usual leisure-time exercise habits.

Calculations

For the first question, weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. Total weekly leisure activity is calculated in arbitrary units by summing the products of the separate components, as shown in the following formula:

Weekly leisure activity score = (9 x Strenuous) + (5 x Moderate) + (3 x Light)

The second question is used to calculate the frequency of weekly leisure-time activities pursued "long enough to work up a sweat" (see questionnaire).

Example

Strenuous = 3 times/wk
Moderate = 6 times/wk
Light = 14 times/wk

Total leisure activity score = (9 x 3) + (5 x 6) + (3 x 14) = 27 + 30 + 42 = 99

Godin Leisure-Time Exercise Questionnaire

1. During a typical **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your free time (write on each line the appropriate number).

Timer PerWeek

a) STRENUOUS EXERCISE
(HEART BEATS RAPIDLY) ______
(e.g., running, jogging, hockey, football, soccer,
squash, basketball, cross country skiing, judo,
roller skating, vigorous swimming,
vigorous long distance bicycling)

b) MODERATE EXERCISE ______
(NOT EXHAUSTING)
(e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)

c) MILD EXERCISE ______
(MINIMAL EFFORT)
(e.g., yoga, archery, fishing from river bank, bowling, Horseshoes, golf, snow-mobiling, easy walking)

2. During a typical **7-Day period** (a week), in your leisure time, how often do you engage in any regular activity **long enough to work up a sweat** (heart beats rapidly)?

OFTEN	SOMETIMES	NEVER/RARELY
1. ☐	2. ☐	3. ☐

APPENDIX I

THE THEORY OF PLANNED BEHAVIOR—LIKERT SCALE

The Theory of Planned Behavior—Likert Scale

Overall, how would you evaluate exercising regularly over the next month? Please use the scale below each item to guide your responses.

	1	2	3	4	5	6	7
a.	Extremely Unenjoyable	Quite Unenjoyable	Slightly Unenjoyable		Slightly Enjoyable	Quite Enjoyable	Extremely Enjoyable
b.	Extremely Harmful	Quite Harmful	Slightly Harmful		Slightly Beneficial	Quite Beneficial	Extremely Beneficial
c.	Extremely Boring	Quite Boring7	Slightly Boring		Slightly Interesting	Quite Interesting	Extremely Interesting
d.	Extremely Foolish	Quite Foolish	Slightly Foolish		Slightly Wise	Quite Wise	Extremely Wise
e.	Extremely Unpleasant	Quite Unpleasant	Slightly Unpleasant		Slightly Pleasant	Quite Pleasant	Extremely Pleasant
f.	Extremely Bad	Quite Bad	Slightly Bad		Slightly Good	Quite Good	Extremely Good

Overall, how much support and approval do you feel you will receive to exercise regularly over the next month? Please use the scale below each question to guide your responses.

1. Most people who are important to me think I should exercise regularly over the next month

1	2	3	4	5	6	7
Strongly Disagree	Moderately Disagree	Slightly Disagree	Neither	Slightly Agree	Moderately Agree	Strongly Agree

2. Most people who are important to me would encourage me to exercise regularly over the next month

1	2	3	4	5	6	7
Strongly Disagree	Moderately Disagree	Slightly Disagree	Neither	Slightly Agree	Moderately Agree	Strongly Agree

3. Most people who are important to me would support me exercising regularly over the next month

1	2	3	4	5	6	7
Strongly Disagree	Moderately Disagree	Slightly Disagree	Neither	Slightly Agree	Moderately Agree	Strongly Agree

Overall, how easy or difficult will it be for you to exercise regularly over the next month? Please use the scale below each question to guide your responses.

1. If you were really motivated, exercising over the next month would be

1	2	3	4	5	6	7
Extremely Hard	Quite Hard	Slightly Hard	Neither	Slightly Easy	Quite Easy	Extremely Easy

2. If you were really motivated, how confident are you that you are capable of exercising regularly over the next month

1	2	3	4	5	6	7
Not at all Confident			Moderately Confident			Extremely Confident

3. If you were really motivated, how much control do you feel you have in exercising over the next month

1	2	3	4	5	6	7
Very little Control			Moderate Control			Complete Control

Overall, do you plan to exercise regularly over the next month? Please use the scale below each question to guide your responses.

1. I intend to exercise regularly over the next month

1	2	3	4	5	6	7
Strongly Disagree	Moderately Disagree	Slightly Disagree	Neither	Slightly Agree	Moderately Agree	Strongly Agree

2. I intend to exercise three times a week over the next month

1	2	3	4	5	6	7
Strongly Disagree	Moderately Disagree	Slightly Disagree	Neither	Slightly Agree	Moderately Agree	Strongly Agree

3. I intend to exercise at least ______ times per week over the next month

APPENDIX J

TOPICS FOR ATTENTION CONTROL GROUP

Topics for Attention Control Group

Comfort rituals for self and family
Talking with your children about a serious illness
Hope and denial
Finding meaning and purpose during health crisis
Fear and anxiety
Depression
Dehydration
Nausea
Mouth care
Caring for yourself and others
Care of the face and head
Sorting out health concerns
Being your own health advocate
Sharing your story
Use of humor in illness
How to deal with worry
Travel to your dream destination (choice of various travelogues to a variety of destinations)
Funniest commercials
Nature videos of various themes
Favorite stand-up comic routines

Example of module:

Finding meaning and purpose in a health crisis:
How have you found or made meaning thus far in your illness? Tell me about this.
Here are some other suggestions that you might want to consider:
Most of us live our lives focused on the future. We make plan for our jobs, our families and our financial security. Illness can disrupt this process. You can feel worried, afraid or uncertain about the future. One can even feel that the illness has removed our ability to plan for the future, which can create a void in our lives. Focusing on the present, instead of the future, can be one new way of finding meaning.

- Focus on today's routines and getting on with them
- Find out what is good about the present moment and try to be grateful for that
- Adjust to simpler tasks or smaller more obtainable goals that give satisfaction

Even though there may be difficult times now, you can still find moments that offer joy, peace and appreciation. A visit from a friend can help you to see value in life even in the midst of a difficult day.

Finding meaning in relationships:
For many people, relationships are central to their understanding of meaning and purpose. These relationships cam be with family, friends, children, grandchildren, siblings and even pets. You can affirm these relationships in many ways:

- Reminisce together
- Talk about how this illness has affected the family and relationships- don't be afraid to talk about your illness, as it gives others permission to do so also
- Enjoy activities together
- Openly express your affection and gratitude to people who are important to you
- Work through treatment decisions and changes/needs
- Let go of old hurts and resentments
- Ask for forgiveness from those you feel you have or disappointed
- Celebrate each birthday, holiday and anniversary in a special way

Finding meaning in artistic activities:
Perhaps you find the works of artists meaningful or do artwork yourself as a way of self expression.

- Enjoy art work that you see from day to day
- Listen to music
- Watch a play or a movie
- Sit in a quiet or sacred place
- Read a favorite poem, novel or biography

Finding meaning in nature:
Illness can confine you indoors, and you can lose connection with nature and you environment.

- Breath fresh air
- Feel the wind, snowflakes or the sunshine on your skin
- Observe the clouds, sunrises and sunsets, the stars or the moon
- Tasting a fresh piece of fruit
- Smelling flowers or the autumn woods
- Sitting outside
- Floating in boat

Knowing that with all your senses you are part of the larger world can give you a sense of meaning knowing that you have a meaningful place in this world and in the big scheme of things. If you are unable to go outside watch an environmental/nature video.

Finding meaning in religion and spirituality:
Many people find meaning and purpose in religion and spirituality. If you consider yourself religious, you may wish to connect with you faith community or develop one

locally while you are getting treatment. Prayer, reading spiritual text and or keeping certain symbols or attending special events can keep you connected. This can also provide some hope and guidance. By staying in touch with what is important to you and your loved ones, you may experience renewed strength and spirit.

Finding meaning in attitude:

Victor Frankl, a Jewish psychiatrist who survived being at Auschwitz, spoke about the importance of the attitude of the person takes toward a fate that cannot be changed. He learned that the human spirit has a defiant power capable of facing the most difficult situations with courage and dignity. He believed that suffering can sometimes give fulfillment and meaning in and of itself.

- Focus on how you want to live in a situation that you cannot change
- Dig deep for strength and inner resources
- Look for good things in any bad situation

Why bother?

Attitude, while it can be hard work sometimes, can make you feel better about your recovery and maybe even cope better!